# Short-term Toxicity Profile of ethanol extract of *Solanum erianthum* leaf in Rats

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## ABSTRACT

**Introduction:** *Solanum erianthum* is medicinal plant used by folklore all over the world. There is no studies conducted on the toxicological effect of the plant. The present study aims to evaluate the toxicological effect of methanol extract of the leaf of the plant. **Methods**: The *Solanum erianthum* leaf was evaluated for toxic effects in Sprague Dawley rats. The extract was given in three doses (125,250,500 mg/kg BW of rats) for 14 days and the effect of the extract on the behaviour and normal physiology was assessed. **Results:** There was no mortality caused in any of the dosage groups. It was observed that the extract not has affected the normal behaviour and caused no deleterious effect on normal physiology, at all the doses given. Extract has no effect on pattern of weight gain and was comparable to normal control group. Serum biochemical parameters also were not altered and were comparable to normal control group. **Conclusion:** The results and observations of study it can be proposed that the extract has no mortality and is completely non toxic to the animal system.

**Key words:** *Solanum erianthum*, 14 days repeated-dose toxicity profile, Hepatic enzymes, Histopathology, Safety profile.

**Citation:** Ramya URS and Lakshmidevi N. Short-term toxicity profile of methanol extract of *Solanum erianthum* leaf in rats. Int J Pharmacol and Clin Sci. 2016;5(4):103-8.

## INTRODUCTION

*Solanum erianthum* is a species of night shade belonging to the family Solanaceae, native to North America and Northern South America. The plant is well known as 'Potato tree' and is characterized by its growth kinetics. Literature indicates that it may be introduced from the Caribbean into West Africa in the era of slave trade to Philippines by the Spanish in the 16th century. From Philippines it may had spread to South-East Asian archipelago, mainland Asia and Australia.[1] The decoction of *Solanum erianthum* leaf has been used locally as diuretic and purgative, to cure malaria, vertigo, leprosy, venereal diseases and it is also taken to stimulate the liver functions. The leaves, as whole powder, are being used for expelling impurities through the urine. Grinded leaves are used as a poultice to treat haemorrhoids and scrofula. Leaves, after heating gently, are applied onto the forehead to treat headache.[2] The decoction of the roots is applied to treat violent body pains or to relieve digestive troubles; it is also given to treat dysentery, diarrhoea and fever. The root bark is used as an antiphlogistic and to treat arthritis. The parts of the plant have been studied and validated for various pharmacological properties.[3] In southern India the fruits are prepared as a curry. In the Philippines the velvety leaves are used to remove grease from dishes. *Solanum erianthum* is considered suitable as a shade plant for coffee, but in Ghana it is considered an undesirable shade plant. In the Caribbean *Solanum erianthum* is planted as an ornamental. Although, the plant has been used in various cultures in various primary health care needs, there is no data regarding the toxic effects, dose and long term side effects of treatment on the animal system. The present study evaluates the effect of 14 days repeated-dose toxicity profile the leaf methanolic extract on normal physiology, biochemistry and behaviour in rats.

**Received :** 01-03-2016 **Revised :** 07-05-2016 ;
**Accepted :** 14-06-2016
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**Conflict of interest:** Nil ; **Source of support :** Nil

**DOI : 10.5530/ijpcs.5.4.2**

Since a very long time medicinal plants have been used as primary health care needs and WHO report indicates developing countries primarily depend on medicinal plants for basic health care.[4] Though medicinal plants contains variety of phytochemicals with beneficial to human health and well being,[5] some of the bio-actives derived from plants may be deleterious to human health.[6] In the process of development of medicinal plant or its derivative(s) as a pharmaceutical, study on the toxicological effects are very crucial. Since toxicological studies evaluate the potential side effects that must be monitored carefully while using as pharmaceutical. The study present study evaluates the toxicity of the *Solanum erianthum* methanol extract.

## MATERIALS AND METHODS

### Chemicals and reagents

Alanine aminotransferase (ALT), Aspartate aminotransferase (AST), Alkaline phosphatase (ALP), Total protein, albumin, urea, creatinine, total bilirubin, tryglycerides, total cholesterol assay kits were purchased from Aggappe Diagnostics,Ernakulam, India. Reduced glutathione (GSH), 5, 5-dithio (bis) nitro benzoic acid (DTNB) were purchased from Sigma-Aldrich, Bangalore, India. All the chemicals and reagents used in the study were of analytical grade.

### Collection and preparation of samples

The leaf of *Solanum erianthum* was collected from Mysore district of Karnataka, India and subsequently identified by Dr. G. R. Shivamurthy, Department of Studies in Botany, University of Mysore, Mysore, India. The collected sample was thoroughly washed under running water to remove adhering dirt and other foreign particles, dried overnight at $50^0$C, powdered, passed through 60 mesh sieve and stored in airtight container at $4^0$C till further use.

**Preparation of the extracts:** The 50 g of leaf powder was extracted with 500 ml methanol for 12 h at 37°C. The extract was filtered using whatsmann filter paper and filtrate obtained was rotary evaporated. Thus obtained greenish brown colored extract was kept at 6-8°C until further use. Yield of the extract was 2.5%.

### Experimental animals

- Sprague Dawley rats (Male and female, 15 each) of 8-9 weeks weighing around 150 gm were selected for the study. 30 rats were kept in polyacrylic cages in the experimental room maintained at a photoperiod of 12 h, humidity of 45 to 60% and temperature of 25 ± 2ºC for acclimatization for one week. Animals were observed for general behavioral conditions in acclimatization period. Standard diet (procured from Amrut feeds, Pune, India) and water *ad libitum* were provided. All the experimental parameters, conditions and procedures followed in the study were approved by Animal Ethical Committee.

### Fourteen days repeated dose toxicity

The animals were grouped into 5 groups Group I – Control; Group II – Vehicle control, group III- SEM treated (150 mg/kg BW), Group IV-SEM treated (250 mg/kg BW), Group V-SEM treated (500 mg/kg BW) using Randomized Block design. The extract was given in the form of suspension of carboxy-methyl cellulose for 14 days. The animals were observed individually after the initiation of dose during first 30 min and at every half an hour interval for 6 hours and thereafter and once in 24 hrs for 14 days. Animals were observed individually for changes in physical or behavioural such as skin and fur, eyes and mucous membrane, respiratory, circulatory, autonomic and central nervous systems and somatomotor activity, behaviour pattern and mortality. Along with the above factors animals were observed for tremors, convulsions, salivation, diarrhoea, lethargy, sleep and coma. After the end of 14 days of study period animals were euthanized and sacrificed.

### Biochemical Estimations

- Animals were euthanized and blood was collected directly from the heart by the method of cardiac puncture. The blood was allowed to coagulate by keeping at 16°C for 4 h. Serum was separated from the coagulated blood by centrifuging. The separated serum was used to assay the activities of alanine amino transferase (ALT), aspartate amino transferase (AST) and alkaline phosphatase (ALP) along with an estimation of total protein, albumin, urea, creatinine, total bilirubin, total cholesterol, triglycerides (TGL) and glutathione (GSH) using respective standard kits.

### Histopathological Procedures

After the animals were sacrificed, liver and kidney were excised and washed with phosphate buffered saline. Some part of the washed liver and kidney were fixed in formalin, dehydrated in graduate ethanol, cleared in xylene and embedded in paraffin. Then the organs which are fixed and embedded in paraffin were thin sectioned (about 4 $\mu$m) and were stained with haemotoxylin and eosin. Stained

**Table 1: 14 days repeated-dose toxicity profile record sheet for control and extract treated animals (n = 6).**

| Drug P.O | Toxicity | | Time of death | Additional observations ANS/CNS | | | | | | | | | | | Behavioural observations | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | onset | stop | | skin & fur | eye lacri | Sali | Diah | Resp | Leth | Sleep | Con | Coma | Ste | Tre | Cat | Geo | Hal | Retr | Stu | Exe |
| Control | nil | nil | 0 | x | x | x | X | X | X | X | X | X | x | X | x | x | x | x | x | x |
| VC | nil | nil | 0 | x | x | x | X | X | X | X | X | X | x | X | x | x | x | x | x | x |
| SEM-150 | nil | nil | 0 | x | x | x | X | X | X | X | X | X | x | X | x | x | x | x | x | x |
| SEM-250 | nil | nil | 0 | x | x | x | X | X | X | X | X | X | x | X | x | x | x | x | x | x |
| SEM-500 | nil | nil | 0 | x | x | x | X | X | X | X | X | X | x | X | x | x | x | x | x | x |

VC-Vehicle control, SEM-150- *Solanum earithum* methanol extract administered at 150 mg/kg BW.SEM-250- *Solanum earithum* methanol extract administered at 250 mg/kg BW.SEM-500- *Solanum earithum* methanol extract administered at 500 mg/kg BW. Lacri; lacrimination; Sali; salivation, Diah; diarrhoea, Resp; respiratory distress, Leth; ethargy, Con; convulsions, Ste; stereotypy, Tre; tremors, Cat; catalepsy, Geo; effect on positive geotropism, Ret; retropulsion, Stu; stupor, Exe; excitement, × - absence of symptom, √ - presence of symptom

**Table 2: Effect of 14 days administration of methanolic extract of *Solanum erianthum* in body weight of rats at different intervals of the study.**

| Groups | Body weight (g) | | |
|---|---|---|---|
| | 1st Day | 8th Day | 14th Day |
| Control | 176.6 ±20.12 | 206.0 ±18.28 | 207.9 ±17.62 |
| VC | 182.8 ±22.12 | 202.1 ±21.92 | 204.9 ±20.59 |
| SEM-150 | 170.7 ±35.11 | 199.4 ±12.90 | 210.0±11.78 |
| SEM-250 | 183.6 ±19.99 | 202.5 ±11.55 | 205.9 ±12.68 |
| SEM-500 | 186.4 ±17.56 | 213.1±17.64 | 214.9±16.28 |

Values expressed are mean of six values with standard deviation, n=6. VC-Vehicle control, SEM-150- *Solanum earithum* methanol extract administered at 150 mg/kg BW.SEM-250- *Solanum earithum* methanol extract administered at 250 mg/kg BW. SEM-500- *Solanum earithum* methanol extract administered at 500 mg/kg BW

**Table 3: Effect of the extract on serum biochemical parameters of various groups**

| Groups | Creatinine (µM/L) | Total protein (g/L) | Albumin (g/L) | Globulin (g/L) | A/G ratio (g/L) |
|---|---|---|---|---|---|
| Control | 54.11±3.39 | 73.55±2.95 | 41.31±2.71 | 33.72±2.98 | 1.548±0.37 |
| VC | 53.4±2.91 | 73.85±3.29 | 42.39±2.49 | 32.31±2.36 | 1.467±0.16 |
| SEM-150 | 52.42±2.68 | 71.84±3.7 | 40.72±1.44 | 31.56±2.4 | 1.215±0.103 |
| SEM-250 | 55.14±2.54 | 72.15±2.39 | 41.29±2.16 | 35.49±2.34 | 1.192±0.06 |
| SEM-500 | 51.52±3.69 | 70.49±3.08 | 40.37±2.04 | 31.53±2.61 | 1.242±0.87 |

Values expressed are mean of six values with standard deviation, n=6. VC-Vehicle control, SEM-150- *Solanum earithum* methanol extract administered at 150 mg/kg BW.SEM-250- *Solanum earithum* methanol extract administered at 250 mg/kg BW. SEM-500- *Solanum earithum* methanol extract administered at 500 mg/kg BW

**Table 4: Effect of the extract on serum liver marker enzyme levels of various groups.**

| Groups | ALT/SGPT | AST/SGOT | ALP | CK | Urea |
|---|---|---|---|---|---|
| Control | 45.88 ±12.19 | 148.7±8.851 | 134.9±5.485 | 207.2±12.89 | 6.918±0.99 |
| VC | 44.38±15.81 | 150.5±8.61 | 137.1±3.6 | 224.9±24.21 | 6.572±0.69 |
| SEM-150 | 43.2 ±15.73 | 161.1±8.39 | 125±4.617 | 202.4±11.06 | 7.132±0.04 |
| SEM-250 | 41.53±10.92 | 149.3±2.733 | 127.2±14.25 | 209.4±14.84 | 7.205±0.75 |
| SEM-500 | 39.85±9.61 | 141.4±17.49 | 146.8±14.67 | 210.4±10.69 | 7.23±0.06 |

Values expressed are mean of six values with standard deviation, n=6. VC-Vehicle control, SEM-150- *Solanum earithum* methanol extract administered at 150 mg/kg BW.SEM-250- *Solanum earithum* methanol extract administered at 250 mg/kg BW. SEM-500- *Solanum earithum* methanol extract administered at 500 mg/kg BW

sections were examined for physiological changes under photomicroscope (400x) and images were taken.

### Statistical analysis

All the expressed values are the mean of triplicate values with ± SD. The data were subjected to a one way ANOVA followed by Tukey's multiple comparison test for significant difference ($p \leq 0.05$) using SPSS 11.5 software.

## RESULTS

### Fourteen days repeated-dose toxicity profile

The treatment with the extract has no deleterious / notable effect on the behavioural pattern and other parameters in rats. Along with the behavioural pattern there were no side effects such as muscle tremor, coma, salivation, vomiting, intake of food pattern, sleeping pattern etc. Table 1 presents the data on toxic symptoms, behaviors and other changes. The extract did not show any toxic symptoms during the whole study period. There were no significant changes in behaviour, ANS or CNS was observed in any of the animals. There were no significant ($p \geq 0.05$) changes in body weights when compared to the control group (Table 2).

### Biochemical Estimations

The serum activities of hepatic enzymes and levels of selected biochemical parameters in serum were represented in Table 3. There was no significant differences in the serum activities ($p \leq 0.05$) of ALP, ALT and AST between experimental and control groups. There was no significant ($p \leq 0.05$) difference observed in biochemical parameters between the test and the control group (Table 4).

### Histology of Liver and Kidney

The liver histological sections of the control and extract treated groups are represented in Figure 1. There were no detectable changes in cellular morphology of hepatocytes, the hepatic architecture was normal with well-defined central vein. No necrosis, steatosis, chronic inflammatory infiltration or degenerative changes were observed in any of the test group animals.

Figure 2. shows the histology of kidney of various groups. There was no alteration from the normal histology of kidney was observed indicating the safety of *Solanum earithum* extract.

## DISCUSSION

Toxicological analysis is a very crucial step in developing a drug using reverse pharmacological approach. Though medicinal history reveals the beneficial pharmacological activities, there will be very less available information on preferred dose, form of the treatment and deleterious side effects. Toxicological analysis of the active extract/ medicinal plant in animal models yields all the above mentioned parameters which are crucial for developing a drug.[8] From ages many medicinal plants are used for traditional treatment. Its availability and cost effectively are added advantages. Presence of rich sources of bioactive compounds in them has made their implications in treatment of several diseases and disorders. Due to lack of research activity, only few medicinal plants have been explored.

The present study deals with the safely of the *Solanum erianthum* in its allowable dosage prescribe by OECD. The study showed no hypersensitivity and allergic reactions when the extract was administered to the rats. During the whole study period they were no behavioural or physical change in the animals. Even the increase in the body weights was compared to normal group.

The metabolic hub of the body is liver, since it maintains and integrates the metabolic activities of the body. If

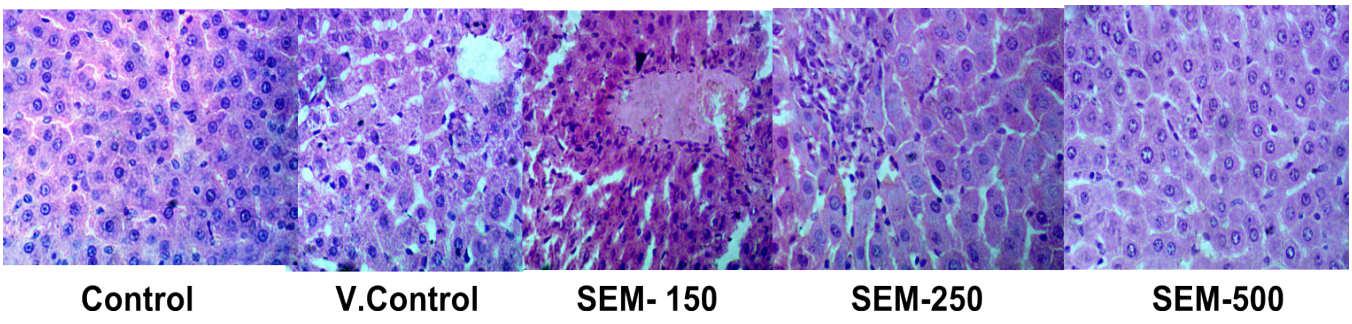


**Figure 1: Liver sections.** V. Control-Vehicle control**,** SEM-150- *Solanum earithum* methanol extract administered at 150 mg/kg BW.SEM-250- *Solanum earithum* methanol extract administered at 250 mg/kg BW. SEM-500- *Solanum earithum* methanol extract administered at 500 mg/kg BW.

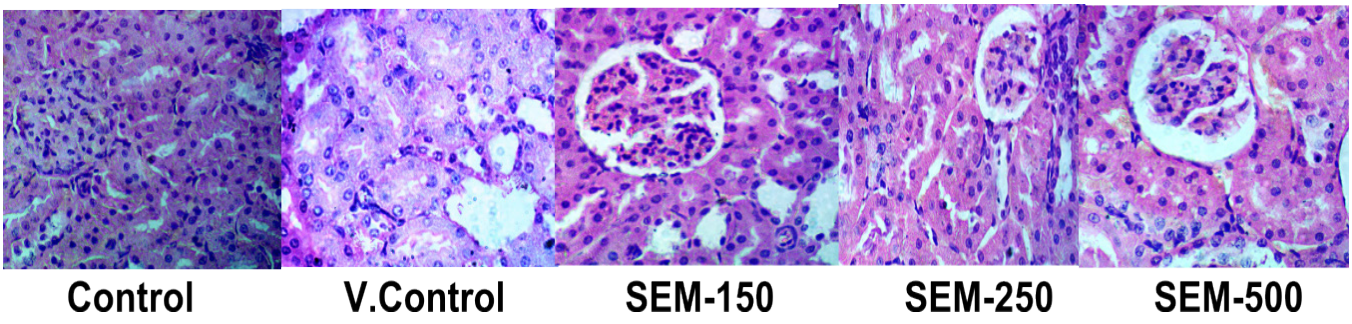


**Figure 2: Kidney sections.** V. Control-Vehicle control**,** SEM-150- *Solanum earithum* methanol extract administered at 150 mg/kg BW.SEM-250- *Solanum earithum* methanol extract administered at 250 mg/kg BW. SEM-500- *Solanum earithum* methanol extract administered at 500 mg/kg BW.

there is any effect/damage to the liver due to any drug treatment, then there will be elevation in serum levels of ALT, AST, ALP and bilirubin. The hepatic enzyme activities and other biochemical parameters assessed in *Solanum erianthum* treated group showed no elevations from normal values. The kidney sections in all the groups showed intact glomerular architecture and basement membrane, the histological structures in the treated group were comparable to normal control group indicating the safety of the extract to the kidney, which was supported by the serum biochemical parameters.

## CONCLUSION

The biochemical, histological and behavioural analysis inferred the safety of the *Solanum erianthum* extract. Hence, it can be concluded that *Solanum erianthum* is non-toxic, non-allergic and the extract alone or as additive in the formulations used in maintain/improving health.

## REFERENCES

1. Mahadev R, Ramakrishnaiah H, Krishna V, Deepalakshmi AP, Kumar NN. Cytotoxic activity of methanolic extracts of *Solanum erianthum* D. Don. International Journal of Pharmacy and Pharmaceutical Sciences. 2014;7(2)106-8.
2. Chandira M, Jayakar B. Formulation and evaluation of herbal tablets containing *Ipomoea digitata* Linn. Extract. Extraction. 2010;3(1):022.
3. Edeoga HO, Okwu DE, Mbaebie BO. Phytochemical constituents of some Nigerian medicinal plants. African Journal of Biotechnology. 2005;4(7):685-8. http://dx.doi.org/10.5897/AJB2005.000-3127.
4. Kumar PP, Kumaravel S, Lalitha C. Screening of antioxidant activity, total phenolics and GC-MS study of *Vitex negundo*. Afr J Biochem Res. 2010;4(7):191-5.
5. Bush BM. Interpretation of laboratory results for small animal clinicians. Blackwell Scientific Publications Ltd; 1991.
6. Little EL, Viereck LA. Atlas of United States trees. US Dept. of Agriculture, Forest Service; 1971.
7. Fabricant DS, Farnsworth NR. The value of plants used in traditional medicine for drug discovery. Environmental health perspectives. 2001;109(Suppl 1):69. http://dx.doi.org/10.2307/3434847 http://dx.doi.org/10.1289/ehp.01109s169; PMid:11250806 PMCid:PMC1240543.
8. Godkar PB, Godkar DP. Textbook of medical laboratory technology. Bhalani publishing house; 2006.
9. Lazarou J, Pomeranz BH, Corey PN. Incidence of adverse drug reactions in hospitalized patients: a meta-analysis of prospective studies. Jama. 1998 Apr 15;279(15):1200-5. http://dx.doi.org/10.1001/jama.279.15.1200 ; PMid:9555760.
10. Britton L, Mills paugh CF. The Bahama flora. New York. 1920:649. PMCid:PMC1362877.
11. Miroslav MG. Elsevier's Dictionary of Trees. London, Elsevier Inc. 2005;1:381. PMid:16229795.
12. Mukherjee Pulok K. Quality control of herbal drugs-An approach to evaluation of botanicals. Bussiness horizons p'ceutical publishers,. 2002:183-213.
13. Mythilypriya R, Shanthi P, Sachdanandam P. Oral acute and subacute toxicity studies with Kalpaamruthaa, a modified indigenous preparation, on rats. Journal of Health science.

2007;53(4):351-8. http://dx.doi.org/10.1248/jhs.53.351.
14. No OT. 423: Acute oral toxicity-acute toxic class method. OECD Guidelines for the Testing of Chemicals. 2001:1-4.
15. Adedapo AA, Adegbayibi AY, Emikpe BO. Some clinico-pathological changes associated with the aqueous extract of the leaves of Phyllanthusamarus in rats. Phytotherapy Research. 2005;1;19(11):971-6.