Available online at www. scholarsresearchlibrary.com

Scholars Research Library

Scholars Research Library

Der Pharmacia Lettre, 2020, 13 (2): 22-29
(http: //scholarsresearchlibrary. com/archive. html)

Der Pharmacia Lettre
Scholars Research Library
ISSN 0975-5071
USA CODEN: DPLEB4

Toxicity Study of Lantana Camara Leaves

Shirish S. Pingale

Department of Chemistry, Gramonnati Mandal's Arts, Com. & Sci. College, Narayangaon, Pune 410504 (Affiliated to University of Pune), India.+91 9890699578

[*]***Corresponding author:*** *Dr. Pingale Shirish S, P.G. Department of Chemistry, Arts, Com. and Sci. College Narayangaon, Junnar, Affiliated to University of Pune, Pune 410504. Contact No: + 91- 9890699578.*
E-mail: drshirishpingale@gmail.com

ABSTRACT

The aim of the present work is to study the toxicity of slurry of dry powder aimed from leaves of Lantana camara. The leaves of this plant were collected from Rajgurunagar, Pune, Maharashtra. The fresh leaves were dried in shade and grinded with high power electric mixer. The dry sample was kept in airtight plastic container and was used for toxicity study as per OECD guidelines by using white albino Wister Rats. The plant material was administered orally at dose of 2 to 10gm/Kg body weight of Swiss mice. The animals were observed continuously for the period of first 4 hours continuously for behavioral changes and then they were kept under observation for 14 days after administration of powder in the form of slurry with the help of gavage. The mortality observations were reported to find out the toxic effect of leaves of Lantana camara. From these results it is observed that Lantana camara leaves powder at doses of 10gm/kg body weight is found to be nontoxic as no any type of abnormal changes were reported in behavior, food and water intake of the administered animals. The Lantana camara plant material was found to be relatively safe when administered orally in Swiss mice. Lethality or adverse toxic signs were not at all observed during the experimental period for our sample.

Keywords: *Lantana camara, Lethality, acute toxicity*

INTRODUCTION

Lantana camara Linn. (Verbenaceae) is an invasive weed, originating from tropical America. It was introduced in several areas, especially in the Australian Pacific region, as an ornamental or hedge shrub. It is used traditionally for the treatment of eczema, rheumatism, leprosy, bilious fever, swellings, ulcers, toothache, stomach ache, influenza, tumours, anaemia, and malaria, and as an antiseptic for wounds. Numerous terpenoids, flavonoids, and steroids have been reported from this plant [1– 8]. Diverse biological features, such as antimicrobial, nematicidal, anticancer, insecticidal, analgesic, anti-inflammatory, anticonvulsant, CNS-depressant, antihyperglycaemic, antimalarial, hepatotoxic, and antihypertensive activities, have been reported for *Lantana camara Linn* [9–12]. Leishmania major is the protozoan parasite, responsible for cutaneous leishmaniasis with an annual incidence rate affecting 1.5 million people globally. According to the World Health Organization (WHO) report, 12 million people are infected by protozoan parasites, while 350 million people are living in the regions with high risk of infection. Drugs containing pentavalent antimony (SbV) are prescribed as the first-line treatment for the leishmaniasis, but they have numerous side-effects. Some of them are reported to be inherently toxic or became ineffective due to resistance developed by parasites against them [13 – 18]. Increasing cases of leishmaniasis in immune compromised patients have been reported. Therefore, there is an urgent need for development of new effective antileishmanial drugs. *Lantana camara Linn*. is a noxious weed belonging to family Verbenaceae which comprise of about 650 species spread over 60 countries. Three varieties of *Lantana camara have* been reported from India in which *L. camara var. aculeate* is the most common [1-4]. The essential oil and extracts of the plant are used in herbal medicines for the treatment of various human diseases such as skin itches, leprosy, cancer, chicken pox, measles, asthma, ulcers, tumors, high blood pressure, tetanus, rheumatism etc.[5,6]. Extracts from leaves have been reported to have antifungal [7 – 9], antiproliferative [10], antibacterial [11-1nematicidal [14], termicidal [15], anthelmintic[16] and anticancer activities[6]. Beside this, the essential oil of the plants also possesses antifungal [17] and antibacterial activities[18,19]. *Lantana camara Linn* whole plant and plant parts have been thoroughly studies for their chemical constituents, previously and recently [6,20-22].All these studies revealed the presence of terpenoids, steroids and alkaloids as major constituents.

The use of natural medicines is increasing and is a persistent aspect of present day health care. More and more people are using herbal medicines as OTC products. There is a belief of many consumers that naturalness is a guarantee of harmlessness, but this is not true. Many traditionally used medicines can produce dangerous and sometimes even lethal poisoning. The world health organization (WHO) is fully aware of the importance of herbal medicines to the health of many people throughout the world. Thus herbal medicines have been recognized as a valuable and readily available resource of primary health care and WHO have endorsed their safe and effective use. A few herbal medicines have withstood scientific testing but others are simply used for traditional reasons to protect, restore and improve health. The WHO has set guidelines for toxicity studies of herbal medicines. It supports appropriate usage of herbal medicines and encourages the remedies, which are proved to be safe and effective. The route for administration for subacute, subchronic and chronic toxicity can be any one of the above stated routes, but most often it is by oral route.

Toxic Dose

Poison is any agent capable of producing a deleterious response in a biological system, seriously injuring function or producing death. Among chemicals there is a wide spectrum of doses needed to produce deleterious effects, serious injury or death. Some chemicals, which produce death in microgram doses, are extremely poisonous, while others may be relatively harmless after doses in excess of several grams.

A chemical agent does not produce toxic effects in biological system unless that agent or its metabolic breakdown (biotransformation) products reach appropriate sites in the body at a concentration and for a length of time, sufficient to produce a toxic manifestation. The major factors which influence toxicity are the route of administration, the duration and the frequency of exposure to the chemical agent. Toxicologists usually divide the exposure of animals into Acute toxicity, Subacute toxicity, Subchronic toxicity, Chronic toxicity [4].

Limit Test

All chemicals can produce toxicity under some experimental conditions, for instance, if a sufficiently large dose is administered. It is therefore, misleading to conduct acute toxicity studies at unreasonably high dose levels for the sake of demonstrating lethality and / or toxicity, which may be irrelevant to the use of compound itself. An extremely high dose of a practically nontoxic compound for example, can cause gastrointestinal blockage, which in turn can result in gastrointestinal tract dysfunction. Toxicity in such a case is not related to the intrinsic characteristic of the test substance, since effect manifested is a direct result of the physical blockage caused by the biologically inert substance. There must be a point, however, at which an investigator may conclude that a test substance is practically nontoxic or nonlethal after an acute exposure. This test limit for oral toxicity generally is considered to be 5.0 g / Kg body weight. If no mortality is observed at this dose level, a higher dose level generally is not necessary [5].

The safety of all medicinal products is of the utmost importance. All applications for new medicines undergo extensive evaluation of their risk to-benefit ratio and, once granted, products are closely monitored for the occurrence of adverse effects. Rabbits fed with edible linguda a low level fern, exhibited systemic toxicity and died following 11 days post feeding. The safety of herbal remedies is of particular importance as most of these products are self-prescribed, available as OTC (over the counter) products and are used to treat minor and often chronic conditions. The trend in the usage of plants as medicines traditionally has enabled one to record the acute and obvious signs of toxicity of the plants, which can be well recognized, and hence their use is avoided

.

MATERIALS AND METHODS

Acute Toxicity Study of Lantana camara leaves powder

An acute toxicity study was carried out for *Lantana camara* leaves by using mice as the experimental model. The study was carried out to assess the acute toxicity of the slurry of leaves powder of *Lantana camara* on oral administration. Study protocol is given below in table **1**.

Table 1: Study Protocol.

Name of the study	**Acute toxicity study**
Test material	*Lantana camara leaves powder*
Animal model	Albino Swiss Mice
Animals procured from	Raj Biotech (INDIA) Ltd., Pune
Sex	Male and Female
Weight range of animals	Between 35 to 55 g
No. of dose groups	Five groups
Animals per group	3 males and 3 females
Route of administration	Intragastric administration with the help of gavage No. 16
Dose volume	2.0 ml per animal
Vehicle for administration	Distilled water
No. of administrations	Single
Concentration of dose	2,4,6,8 and 10gm/Kg body weight
Study duration	Acclimatization for 14 days, one day drug administration and 14 days observation period including holidays
Parameters observed	Cage side observations, daily food and water intake, daily body weight and daily mortality record etc

Animal Maintenance

The animals were housed in polyurethane cages. The cages were provided with rice husk bedding and were cleaned daily. The animals were provided with drinking water ad libitum and were fed on commercially available Mice feed supplied by AMRUT FEED. The specifications of the feed are listed below in table **2.**

Table 2: Composition of feed.

Name	**Percentage**
Crude Protein	20 - 21 % minimum
Ether Extractive	04 - 05 % minimum
Crude Fiber	04 % maximum
Ash	08 % maximum
Calcium	1.2%
Phosphorus	0.6 % minimum
NFE	54 %
ME Kcal/Kg	3600
Pallet Size	12 mm

The feed was enriched with stabilized vitamins such as Vit. A and D_3, Vit. B_{12}, Thiamine, Riboflavin, Folic acid and supplemented with all minerals and microelements. Measured quantities of water and feed were supplied daily in each cage. The consumption of water and food was estimated from the amount of water remaining in feeding bottles and from the amount of feed remaining in the feed hopper.

RESULTS AND DISCUSSION

Cage Side Observations

Assessment of the behavior of animals was carried out by general observations of each animal on a daily basis from the stage of dosing to the end of the study. Cage-side observations included daily recording of condition of the fur; damaged areas of skin; subcutaneous swellings or lumps (the size, shape and consistency), areas of tenderness, abdominal distension, eyes - for dullness, discharges, opacities, pupil diameter, ptosis (drooping of upper eyelid), the colour and consistency of the faeces, wetness or soiling of the perimenum, condition of teeth, breathing abnormalities, gait, etc. Any changes or abnormalities recorded could be an indication of toxicity.

The test animals at all dose levels showed no significant changes in behavior before and after the administration of an oral dose of *Caesalpinia bonducella* decoction in the form of slurry following table **3** shows the dosage regime. Table **4** shows the observations for the parameters studied. Table **5** shows the mortality record.

Table 3: Doses Regime.

Sr. No.	Sex	Dose gm./Kg Body Wt.	No. of animals used	Total Vol. administered in cm3
1	Male	2	3	2
2	Female	2	3	2
3	Male	4	3	2
4	Female	4	3	2
5	Male	6	3	2
6	Female	6	3	2
7	Male	8	3	2
8	Female	8	3	2
9	Male	10	3	2
10	Female	10	3	2

Table 4: Cage Side Observations for all animals.

Sr. No.	Parameters	Cage Side Observations
1	Condition of the fur	Normal
2	Skin	Normal
3	Subcutaneous swellings	Nil
4	Abdominal distension	Nil
5	Eyes-dullness	Nil
6	Eyes-opacities	Nil
7	Pupil diameter	Normal
8	Ptosis	Nil
9	Colour and consistency of the faeces	Normal
10	Wetness or soiling of the perimenum	Nil
11	Condition of teeth	Normal
12	Breathing abnormalities	Nil
13	Gait	Normal

Table 5: Mortality Record.

Group ml/Kg	**2**	**2**	**4**	**4**	**6**	**6**	**8**	**8**	**10**	**10**
Sex	**Male**	**Female**	**Male**	**Female**	**Male**	**Female**	**Male**	**Female**	**Male**	**Female**
Hr. 1	-	-	-	-	-	-	-	-	-	-
Hr. 2	-	-	-	-	-	-	-	-	-	-
Hr. 3	-	-	-	-	-	-	-	-	-	-
Hr. 4	-	-	-	-	-	-	-	-	-	-
Day 1	-	-	-	-	-	-	-	-	-	-
Day 2	-	-	-	-	-	-	-	-	-	-
Day 3	-	-	-	-	-	-	-	-	-	-
Day 4	-	-	-	-	-	-	-	-	-	-
Day 5	-	-	-	-	-	-	-	-	-	-
Day 6	-	-	-	-	-	-	-	-	-	-
Day 7	-	-	-	-	-	-	-	-	-	-
Day 8	-	-	-	-	-	-	-	-	-	-
Day 9	-	-	-	-	-	-	-	-	-	-
Day 10	-	-	-	-	-	-	-	-	-	-
Day 11	-	-	-	-	-	-	-	-	-	-
Day 12	-	-	-	-	-	-	-	-	-	-
Day 13	-	-	-	-	-	-	-	-	-	-
Day 14	-	-	-	-	-	-	-	-	-	-
Mortality	0/3	0/3	0/3	0/3	0/3	0/3	0/3	0/3	0/3	0/3

Body Weight Changes

Body weight is an important factor to monitor the health of an animal. Loss in body weight is frequently the first indicator of the onset of an adverse effect. A dose, which causes 10 % or more reduction in the body weight, is considered to be a toxic dose. It is considered to be the dose, which produces minimum toxic effect, irrespective of whether or not it is accompanied by any other changes. All the animals from treated groups did not show any significant decrease in body weights for all the 14 days as compared with the 0 day values, indicating no signs of toxicity against powder of leaves of *Lantana camara*. The variation in body weight changes of males and females and the data is given in Table **6.**

Table 6: Daily Body Weight Record in Grams.

(All the values expressed as mean of three animals in each group)

Group gm/Kg	**2**	**2**	**4**	**4**	**6**	**6**	**8**	**8**	**10**	**10**
Sex	**Male**	**Female**	**Male**	**Female**	**Male**	**Female**	**Male**	**Female**	**Male**	**Female**
Day 0	54	35	45	37	36	46	55	46	55	36
Day 1	54	34	45	36	36	45	56	46	56	36
Day 2	55	35	45	37	36	46	56	47	55	36
Day 3	55	36	46	37	36	46	56	47	54	34
Day 4	51	35	44	36	35	46	55	46	55	35
Day 5	55	35	46	38	38	46	57	47	55	36
Day 6	55	36	46	37	38	46	57	47	56	36
Day 7	56	36	45	38	38	46	58	48	55	36
Day 8	55	36	46	38	37	47	58	48	56	36
Day 9	54	34	45	38	37	45	57	47	54	36
Day 10	54	36	46	38	37	45	56	46	55	35
Day 11	56	38	46	39	37	47	57	48	56	38
Day 12	55	37	46	39	39	46	55	45	47	39
Day 13	47	43	44	49	48	45	47	48	48	49
Day 14	43	42	44	49	47	48	48	49	47	48

Table 7: Daily Food Intake Record in Grams.

(All the values expressed as mean of three animals in each group)

Group gm/Kg	2	2	4	4	6	6	8	8	10	10
Sex	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
Day 0	15	11	16	14	21	14	16	14	11	16
Day 1	16	12	16	14	21	14	16	14	12	16
Day 2	15	12	16	14	21	14	16	14	12	16
Day 3	16	11	16	14	22	14	16	14	11	16
Day 4	15	10	15	14	20	15	15	14	10	15
Day 5	17	12	17	15	22	14	17	15	12	17
Day 6	17	12	17	14	22	14	17	14	12	17
Day 7	18	12	18	14	22	15	18	14	12	18
Day 8	18	11	18	14	22	15	18	14	11	18
Day 9	19	11	18	14	23	13	18	14	11	18
Day 10	17	15	14	17	16	15	17	18	17	19
Day 11	16	15	14	15	16	15	16	17	16	18
Day 12	15	10	15	14	20	15	15	14	10	15
Day 13	17	17	15	16	16	15	17	17	16	16
Day 14	18	14	15	17	17	16	16	17	16	18

Food and Water Consumption

There was no significant change in food and water intake of the test animals at all dose levels. The data for food and water consumption is given in Tables 7 and 8 respectively.

Table 8: Daily Water Intake Record in ml.

(All the values expressed as mean of three animals in each group)

Group gm/Kg	**2**	**2**	**4**	**4**	**6**	**6**	**8**	**8**	**10**	**10**
Sex	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
Day 0	13	11	15	14	20	13	14	11	11	15
Day 1	12	11	15	14	20	13	14	11	11	15
Day 2	13	12	14	13	19	14	13	12	12	14
Day 3	14	12	14	13	21	14	13	12	12	14
Day 4	14	12	14	15	21	14	15	12	12	14
Day 5	15	13	13	15	21	14	15	13	13	13
Day 6	13	12	15	14	20	13	14	12	12	15
Day 7	14	12	15	14	22	11	14	12	12	15
Day 8	15	12	16	14	22	12	14	12	12	16
Day 9	15	11	15	14	22	12	14	11	11	15
Day 10	14	12	16	13	23	12	13	12	12	16
Day 11	15	11	16	13	21	12	13	11	11	16
Day 12	16	12	17	14	23	13	14	12	12	17
Day 13	17	11	17	13	22	13	13	11	11	17
Day 14	17	11	18	14	23	12	14	11	11	18

Mortality

Mortality is the main criteria in assessing the acute toxicity (LD_{50}) of any drug. There was no mortality recorded even at the highest dose level i.e. 10gm/ Kg. body weight.

CONCLUSION

From the results of this study, it is observed that there is no considerable change in body weight, food and water consumption by the animals from all dose groups (2gm/Kg body weight to 10gm/Kg body weight), There was no mortality recorded even at the highest dose level i.e. 10gm/Kg body weight, which proves that the powder of leaves of *Lantana camara* of this plant has no significant toxic effect in mice.

REFERENCES

[1] The Wealth of India: Raw Material, Publication & Information Directorate, CSIR, New Delhi, India.1972: VI: p. 31-34.
[2] Morton, JF., Lantana camara L,Verbenaceae , Econ Bot 1994. 48(3):p. 259-270.
[3] McLennan, MW. and Amos, ML., Australian Veterinary Journal, 1989. 66(3): p.93-94.
[4] Ross, IA., Medicinal plants of the world 1999. 3(4): p.325-335.
[5] Ghisalberti, EL., Lantana camara Linn,2012. 71(5):p.467-485.
[6] Tripathi, AK., and Shukla, BNc., Plant Pathol, 2020. 32(6): p.266-267.
[7] Kumar, VP., J Ethnopharmacol, 2006. 107(2): p.182-188.
[8] Srivastava, D., and Singh, p., Asian Journal of Experimental Biological Science, 2011. 2(3): p. 525-528.

[9] Mostafa, AA., Al-Rahmah, AN., and Abdel, MA., Journal of Medicinal Plant Resarch, 2011. 5(17): p.4231-4238.

[10] Hussain, T., Arshad, M., Khan, S., Sattar, H., and Qureshi, MS. Pakistan Journal of Botany, 2011. 43(1):p. 531-538.

[11] Mary, KV., Plant Sciences Feed, 2011. 34(3):p. 74-79.
[12] Mani, LM., et al., Scholars Research Library, 2010. 2(5):p. 80-82.
[13] Barreto, FS., et al.,Jornal of Young Pharmacists, 2010. 2(1):p. 42-44.
[14] Verma, RK., and Verma, SK., Fitoterapia, 2006. 77(6):p. 466- 468.
[15] Bequm, S., Siddiqui, BS., and Wahab A., Natural Product Research, 2008. 22(6):p. 467-470.
[16] Mohapatra, TK., International Resarch Pharmacy Science, 2011. 2(1):p. 12-15.
[17] Sonibare, OO., and Effiong, I., African Journal Biotechnology, 2008. 7(15):p. 2618-2620.
[18] Pattnaik, S., and Pattnaik, B., International Research Journal Pharmaceutical Sciences, 2017. 10(3):p. 32-35.
[19] Tesch, NR., Natural Product Communications, 2011. 6(7):p. 1031-1034.
[20] Kurade, NP. Et al., Pharmaceutical Biology, 2010. 48(5):p 539-544
[21] Miguel,G., et al., Jornal of the Chilean Chemical Society, 2009. 54(4):p. 379-384.
[22] Padalia, RC., Verma, RS., and Sundaresan, V., Records Natural Products, 2010. 4(2):p. 109-114.
[23] Montanari, RM., ET AL., Quim Nova, 2011. 34(9): p. 1550-1555.
[24] Sousa, EO., et al., Records of Natural Products, 2012. 6(2):p. 144-150.
[25] Sousa, EO., et al., Records of Natural Products, 2010. 4(1):p. 31-37.
[26] Saikiya, AK., and Sahoo, RK., Middle-East Journal of Scientific Research, 2010. 48(5):p. 539-544.
[27] William Blake., Journal of the American Pharmaceutical, 1950. 30(4):p. 316-319.
[28] Adams,RP., Identification of essential oil components by gas chromatography/mass spectrometry (4th Ed.). Allured Business Media, Carol Stream, IL, U.S.A. 2009. P.131-140
[29] Rowlling,JK., World Health Organisation Regional Office for the Western Pacific Manila, 1993. 1(9): p. 156-167.
[30] John, HD. Howard,GJ, and John,HD., Fundamental Toxicology for Chemists,1996. 12(6) : p. 1-24.
[31] Shirish, SP., The Basic Science of Poison, 2019. 9(3): p. 2249-2256.
[32] Trevan, JW., Proceeding of the Royal Society of London, 1927. 101(712):p. 721-734
[33] Karl May.,Background on acute toxicity testing for chemical safety, August, 1984 .p.176-190.
[34] Hans Aanrud.,Final report on acute studies workshop, 1983.p. 767-770.

Body Weight Changes

Body weight is an important factor to monitor the health of an animal. Loss in body weight is frequently the first indicator of the onset of an adverse effect. A dose, which causes 10 % or more reduction in the body weight, is considered to be a toxic dose. It is considered to be the dose, which produces minimum toxic effect, irrespective of whether or not it is accompanied by any other changes. All the animals from treated groups did not show any significant decrease in body weights for all the 14 days as compared with the 0 day values, indicating no signs of toxicity against powder of leaves of *Lantana camara*. The variation in body weight changes of males and females and the data is given in Table **6.**

Table 6: Daily Body Weight Record in Grams.

(All the values expressed as mean of three animals in each group)

Food and Water Consumption

There was no significant change in food and water intake of the test animals at all dose levels. The data for food and water consumption is given in Tables **7** and **8** respectively.

Table 8: Daily Water Intake Record in ml.

(All the values expressed as mean of three animals in each group)

Mortality

Mortality is the main criteria in assessing the acute toxicity (LD_{50}) of any drug. There was no mortality recorded even at the highest dose level i.e. 10gm/ Kg. body weight.

CONCLUSION

From the results of this study, it is observed that there is no considerable change in body weight, food and water consumption by the animals from all dose groups (2gm/Kg body weight to 10gm/Kg body weight), There was no mortality recorded even at the highest dose level i.e. 10gm/Kg body weight, which proves that the powder of leaves of Lantana camara of this plant has no significant toxic effect in mice

REFERENCES