Indian Journal of Fundamental and Applied Life Sciences ISSN: 2231– 6345 (Online)
An Online International Journal Available at http://www.cibtech.org/jls.htm
2024 Vol. 14, pp. 1-5/Indira and Hamsa
Review Article (Open Access)

A REVIEW ON THE PHARMACOLOGICAL TOXICITY OF *LANTANA CAMARA* (LINN.) IN RUMINANTS

***M.N. Indira and B.M. Hamsa**
Department of Life Sciences, Kristu Jayanti College, Autonomous, Bengaluru 560077
**Author for Correspondence: indiramn@gmail.com*

ABSTRACT
Lantana camara is regarded as a toxic and invasive weed in many parts of the world. The plant may be grazed by ruminants and ingestion of large quantities of lantana may lead to acute toxicity. Lantadenes are the major toxic triterpenes found in the immature fruits and leaves of *lantana* which cause injury to the animals. Liver and kidneys are the most affected organs during lantana poisoning leading to hepatotoxicity and photosensitization. The cattle may die from severe ruminal stasis and cholestasis. No specific antidote is available against lantana toxicity. Through proper and timely preventive measures, the toxicity of lantana can be managed. This review focuses on the symptoms, diagnosis and treatment of lantana poisoning in ruminants.

Keywords: *Lantana, Toxicity, Lantadene, Choleostasis, Ruminants, Cattle*

INTRODUCION
Lantana camara (Verbenaceae) is an attractive shrub often referred as red sage or yellow sage. Originally native to tropical America, they have expanded to numerous tropical and subtropical regions across the globe due to its weedy characteristics (Stegelmeier *et al.,* 2013; Kato-Noguchi and Kurniadie, 2021). They are widely distributed in Northern parts of India, Uttar Pradesh, several parts of Maharashtra and South India as well (Kalita *et al.,* 2012). Several related species of lantana such as *L. indica, L. crenulata, L. trifolia, L. lilacina, L. involucrata, L. sellowiance including L. camara* are poisonous to animals. The toxicity of different cultivar varies greatly. Red and yellow flowered varieties pose a significant risk to animals, pets and cattle (Govindaiah *et al.,* 2021). Its toxicity is reported in a number of domestic and grazing animals that include dogs, cats, cattle, sheeps, goats, guinea pigs, horses, ostriches, camels, rats and rabbits (Kumar *et al.,* 2018; Ambica *et al.* 2020; Nagy *et al.,* 2023). Cases of lantana poisoning in ruminants are extremely common in Southern Rajasthan (Katewa *et al.* 2008; Singh 2018; Tarunpreet and Saganpal, 2021). In most of South Africa's semi-arid regions, the growth of *L. camara* also poses a threat to the lives of cattle and sheep (Ntalo *et al.,* 2022).

Grassland ruminants avoid ingesting of lantana due to its strong odor and taste. The majority of lantana poisoning cases involve animals that are not familiar with the plant being allowed to graze in lantana weed-filled areas. Accumulation of more than one percent of toxic content than the body weight of the animal may cause toxicity depending on the quantity of the lantana eaten (Shafi *et al.,* 2020). Animals are more poisoned by the immature fruits and leaves of lantana (Haritha *et al.,* 2019). Lantadenes, which are pentacyclictriterpenoids, are the active substances that cause lantana poisoning in ruminants. Significant pentacyclic triterpenes, icterogenin, lantadene A and lantadene C are the most poisonous and prevalent (Cullen and Stalker, 2016). The red flower of lantana mostly contain lantadene A, B, C and D. Goats are somewhat immune to the lantadenes, but ruminant animals like sheep, cattle, and buffalo are very susceptible to them (Sharma *et al.,* 2007; Pour, 2011).

Allelopathy is one of the main factors that contribute to *L. camara's* invasiveness. Extracts from *L. camara*, essential oil, leachates, residues, and rhizosphere soil containing phenolic chemicals, sesquiterpenes, triterpenes, and a flavonoid impede the germination and growth of other plant species. The most phytotoxic compounds are salicylic acid, methylcoumarin and umbelliferone (Kato-Noguchi and Kurniadie, 2021). According to a recent study, lantadene A (Rehmannic acid.) and B are more potent allelochemicals than phenolics (Sharma *et al.,* 2007). In addition, it contains various phytochemicals such as alkaloids, glycosides, saponins, steroids, carbohydrates and coumarins which contribute to its medicinal and healing properties (Kalita *et al.,* 2012; Al-Snafi

2019; Naz and Bano, 2013; Maroyi, 2021). The poisonous triterpenes are absorbed through the gastro intestinal tract degenerate the liver in cattle, resulting in symptoms such as depression, rumen stasis, jaundice, and photosensitization (Blowey and Weaver, 2011).

Signs and symptoms of lantana toxicity

Symptomatic indications of lantana toxicity typically appear after a few days after ingestion of dangerous plants. A ruminant's symptoms may vary depending on the kind and amount of lantana it eats as well as how much sunlight the animal is exposed to. In severe situations, symptoms may show up within 24 hours of a single feeding. Sheep and cows are the normal species impacted. Cattle may develop lesions near their mouths, noses and muzzles. Swelling of ears and eyelids with discharge from eyes are observed. The cheeks, tongue, and gums may be affected by ulceration, while the nostrils may experience swelling, hardening, and peeling of deeper tissues and mucous membranes is reported (Sebastian, 2007).

Chronic cholestasis, commonly seen in sheep, goats, and horses, is the most common symptom of *L. camara* poisoning in grazing animals. It is characterised by severe icterus and photosensitization. The new born ruminants show some of resistance by prolonging the ruminant's exposure to poisons by retaining the plant in the rumen (Cullen and Stalker, 2016). Lantana toxicity may involve three stages such are: absorption and release of toxins by the gastrointestinal tract; cholestasis, hyperbilirubinemia, hyperphylloerythrinemia of the liver, accumulation of phylloerythrin and bilirubin resulting in cell damage (Sharma *et al.,* 1988). Reports have shown an outbreak of lantana poisoning in cattle that sought shelter in a eucalyptus forest that was invaded by *Lantana camara.* Some of the poisoned animals died, including a few heifer bulls, while others had lethargy, increased serum activity of hepatic enzymes, extreme photosensitivity, jaundice, hepatomegaly, and nephrosis. Clinical examination revealed dullness, fever, reduced ruminal motility, pale and yellow mucus membrane, and photosensitisation in the bulls (Baruthi *et al.,* 2018). The Sirohi goats that grazed on lantana experienced constipation followed by diarrhoea, dehydration, icteric mucous membrane, and weakness in their hind limbs. Observations included alopecia, erythema, oedema, and irritation on the hairless area. There was also sloughing of the epidermis with discomfort in the sun (Meena *et al.,* 2022). Similar signs of lantana poisoning were reported earlier in Jersey crossbred cattle (Srikanth and Kumar, 2013). The other histological changes observed are arbitrary cholestasis, biliary proliferation, hepatocellular necrosis, and centrilobular necrosis. Machado *et al.,* 2023).

Cholestasis bile canalicular injury and hepatotoxic effects

Lantana poisoning may induce hepatotoxic effects in ruminants and is characterized by cholestasis (Sharma *et al.,* 2007; Varga and Puschner, 2012). In sheep, oral administration of the poisonous lantana triterpene decreased lantadene A, caused intrahepatic cholestasis linked to bile canalicular damage. 85% of the lantana toxins that was injected into a sheep's portal vein was eliminated through its bile. Triterpene metabolites likely interacted with bile canalicular membrane components to cause cholestasis (Pass and Goosem, 1983). It has previously been reported that in cattle, sheep, and goats, Lantadene A causes bile canal damage, intrahepatic cholestasis, and jaundice (Deepa *et al.,* 2017).

Steatosis from *Lantana camara* results in cholestasis and hepatocyte enlargement. The hepatocytes are affected by triterpene toxins like lantadene A and B. The canaliculi appear to be the primary site of damage. A few hours after ingesting the plant, there is a reduction in canalicular ATPase activity and a collapse of canaliculi (Pass *et al.,* 1978).

Pentacyclic triterpenoids irritate the gastrointestinal tract and are hepatotoxic (Sharma *et al.,* 2007). Reports have indicated the occurrence of severe acute centrilobular necrosis of the liver when administered at large dosages. According to Johnson and Jensen study, Red kangaroos that consumed *L. camara* extract suffered liver damage. Liver damage includes hepatomegaly and orange staining of the liver (Nagy *et al.,* 2023). Lantadene A and B also have a significant hepatotoxic effect on the non-ruminants too (Pour *et al.,* 2011).

Sheep, goats and bovines exhibited photosensitisation. In ruminants, obstructive cholangitis causes bilirubin and phylloerythrin retention, which results in photosensitization (Nagy *et al.,* 2023). Grazing calves that have eaten enough of the plant, experience photosensitisation, which is characterised by

liver damage and an accumulation of phylloerythrin in the blood, which makes the skin of the animal more sensitive to ultraviolet light.
There is significant inflammation on the skin, in the eyes, and around the genital orifices, and the nasal and face regions are severely affected (Govindaiah *et al.,* 2021). Pathological symptoms in experimental animals showed elevated serum urea and creatinine concentrations. The affected cattle became jaundiced and voided soft, black faeces. Acute poisoning also led to the death of cattle (Fourie *et al.,* 1987).

Gastrointestinal effects and paralysis of gall bladder
An often seen pathological alteration in sick animals is the blockage of the gastrointestinal mucosa as a result of lantana irritation. The bile canalicular membranes and microvilli are harmed by the triterpenoids, which prevents ATPase function and impedes bile flow. In chronic cases, microscopic findings have included ductal response, portal fibrosis, and centrilobular necrosis. Additionally seen are gallbladder enlargement and wall oedema (Nagy *et al.,* 2023). A few hours after lantana is administered, rumen stagnation sets in, and the flow of ingesta into the small intestine reduces in accordance with reports on rumen motility (Gupta *et al.,* 2019). It has been shown that sheep intoxicated with lantana retain significant levels of toxins in their stagnant rumen, creating a toxic reservoir from which continuous absorption sustains the sickness (McSweeney and Pass, 1983).
The accumulation of endogenous chemicals like lantadene A and bile salts may be the cause of paralysis and lack of gall bladder motility. Bile salts were able to suppress the compression of sheep gallbladder sections in vitro in response to cholecystokinin, pentagastrin, and acetylcholine; however, lantadene A only prevented the withdrawals to cholecystokinin (Pass and Heath,1978; Morton, 1994).

Post-mortem symptoms
Yellow discolouration of tissues, hard, dry, mucus-covered faecal lumps in the large intestine, and dry, undigested plant material in the rumen were among the postmortem signs in ruminants. There appears to be swelling in the kidney, gall bladder, and liver. Additionally, a moderate to diffuse pulmonary congestion was noted. Faeces were found in the colon and rectum, indicating constipation. (Gupta *et al.,* 2019). Pale mucous membranes, acute icterus, dehydration, constipation, an enlarged liver, a distended gallbladder with dark, opaque, and sticky contents were all observed during the necropsy of goats poisoned with lantana. The kidneys became necrotic. Putty-like faeces also affected the colon and rectum. Additional signs and symptoms include splenic and pulmonary congestion (Meena *et al.,* 2022).

DIAGNOSIS AND TREATMENT

Diagnosis of lantana poisoning is based on the history, clinical symptoms and post-mortem findings. Severe poisoning or delayed diagnosis may lead to death of the animals (Meena *et al.,* 2022). There is no specific antidote discovered yet. Management of lantana toxicity through preventive actions and supportive therapy have proven to be effective in the treatment (Oyouroua *et al.,* 2013). Activated charcoal is a fast-acting, affordable, and efficient counter-measure. If the animal has not improved 24 hours after the initial dosage, a second dose may be necessary. Toxins in the rumen are adsorbed by activated charcoal, which also stops the body from absorbing further toxins. Although it takes longer to work than charcoal, bentonite is less expensive (Gupta *et al.,* 2019; Haritha *et al.,* 2019).
Jaundice can be effectively treated with oral liver tonics, vitamin B complex medication, and bilirubin-oxidase enzyme elimination of bilirubin (McSweeney and Pass, 1982; Sharma *et al.,* 2007). According to a case study by Baruthi *et al.,* (2018), intravenous saline treatment was required to rehydrate bulls that had been poisoned with lantana. The ruminal content was removed by purging with magnesium sulphate ($MgSO_4$). Application of topical ointments over the affected areas, antihistamine injections supplemented with liver tonics are found to be effective. Providing hydration therapy, keeping intoxicated animals away from light, and providing enough food are some common conventional therapeutic techniques that can be used.

CONCLUSION

Depending on the kind of mammal or livestock, lantadenes, are the main active substances that cause lantana poisoning in ruminants. They are mostly found distributed in the plant's leaves and can have detrimental consequences when consumed. It can be concluded that symptoms of *Lantana camara* poisoning can be effectively alleviated with appropriate and prompt supportive treatment. But, precautionary steps should always be taken since they can greatly reduce the possibility of poisoning. More pharmacological, phytochemical, and toxicological research on lantana is further necessary to evolve an effective antidote for lantana intoxication.

CONFLICT OF INTEREST

The authors declare no conflicts of interest related to this manuscript.

REFERENCES

Al-Snafi AE (2019). Chemical constituents and pharmacological activities of *Lantana camara* – a review. *Asian Journal of Pharmaceutical and Clinical Research,* **12**(12) 10-20.

Ambica G, Reddy GAK, Banotha AK and Kumar SR (2020). Therapeutic management of Lantana associated hepatic and renal toxicity in a bullock: a case report. *Journal of Entomology and Zoological Studies,* **8**(2) 1502-04.

Baruti M, Singh B, Bhuyan M, Borthakur A, Bhuyan D and Chutia JP (2018). Management of *Lantana camara* poisoning in a bull. *International Journal of Chemical Studies,* **6**(1) 950-952.

Cullen JM and Stalker MJ (2016). Liver and biliary system. In: *Jubb, Kennedy & Palmer's Pathology of Domestic Animals,* Vol 2, 6th edn. 258-352e1. [Online] Feb 5. doi: 10.1016/B978-0-7020-5318-4.00008-5

Deepa C, Rajan SK and Nikhila M (2017). Acute *Lantana camara* poisoning in goats- a case report. *Journal of Indian veterinary Association,* **15**(2) 34- 35.

Fourie N, Van der Lugt JJ, Newsholme SJ and Nel PW (1987). Acute *Lantana camara* toxicity in cattle. *Journal of the South African Veterinary Association,* **58**(4) 173-8.

Govindaiah K, Biradar R, Gupta VMD and Munivenkatappa BS (2021). Lantana toxicity in grazing cattle. *Indian Journal of Veterinary Sciences and Biotechnology,* **17**(1) 85–88.

Gupta RK, Niyogi D, Nayan R, Singh SV, Mishra A and Varun VK (2019). Clinico-pathological study of *Lantana camara* toxicity in a sheep farm. *Journal of Pharmacognosy and Phytochemistry* **8**(4) 2219-2221.

Haritha CV, Khan S, Manjusha KM and Banu A (2019). Toxicological aspects of common plant poisoning in ruminants. *Indian Farmer,* **6**(11) 812-822.

Kumar R, Sharma R, Patil RD, Mal G, Kumar A, Patial V, Kumar P and Singh B (2018). Sub-chronic toxico pathological study of lantadenes of *Lantana camara* weed in guinea pigs. *BMC Veterinary Research,* **14**(1) 129.

Kalita S, Kumar G, Karthik L and Rao KVB (2012). A review on medicinal properties of *Lantana camara* Linn. *Research Journal of Pharmacy and Technology,* **5**(6) 711-15.

Katewa SS, Galav PK, Nag A and Jain A (2008). Poisonous plants of the southern Aravalli hills of Rajasthan. *Indian Journal of Traditional Knowledge,* **7**(2) 269-272.

Kato-Noguchi H and Kurniadie D (2021). Allelopathy of *Lantana camara* as an invasive plant. *Plants* **10**(5) 1028.

Oyouroua JN, Combrincka S, Regnier T and Marstonb A (2013). Purification, stability and antifungal activity of verbascoside from *Lippia javanica* and *Lantana camara* leaf extracts. *Industrial Crops and Products,* **43** 820-826.

Machado M, Oliveira LGS, Schild CO, Boabaid F, Lucas M, Buroni F, Castro MB Aand Riet-Correa F (2023). *Lantana camara* poisoning in cattle that took refuge during a storm in a forest invaded by this plant. *Toxicon,* **229** 107124.

Maroyi A (2021). Pharmacological properties and medicinal applications of *Lantana rugosa* Thunb. (Family Verbenaceae). *Research Journal of Pharmacy and Technology,* **14(1)** 259-264.

McSweeney CS and Pass MA (1983). The role of the rumen in absorption of Lantana toxins in sheep. *Toxicon* **21** 285-288.

Meena VK, Meena S and Choudhary SD (2022). Lantana Poisoning in Sirohi goats in Bojunda, Chittorgarh *Haryana Veterinarian*, **61**(SI) 128-130.
Morton JF (1994). Lantana, or red sage (*Lantana camara* L., [Verbenaceae]), notorious weed and popular garden flower; some cases of poisoning in Florida. *Economic Botany*, **48** 259–70.
Nagy AL, Ardelean S, Chapuis RJJ, Bouillon J, Pivariu D, Dreanca AI and Caloni F (2023). Emerging plant intoxications in domestic animals: A European perspective. *Toxins*, **15**(7) 442.
Naz R and Bano A (2013). Phytochemical screening, antioxidants and antimicrobial potential of *Lantana camara* in different solvents. *Asian Pacific Journal of Tropical Disease* **3**(6) 480–86.
Ntalo M, Ravhuhali KE, Moyo B, Hawu O and Msiza NH (2022). *Lantana camara*: Poisonous species and a potential browse species for goats in Southern Africa—A review. *Sustainability* **14**(2) 751.
Pass MA and Heath TA (1978). The effect of *Lantana camara* on intestinal motility in sheep. *Journal of Comparative Pathology*, **88**(1) 149-56. [Online] doi: 10.1016/0021-9975(78)90071-3.
Pass MA, Seawright AA, Heath TJ and Gemmell RT (1978). Lantana poisoning: a cholestatic disease of cattle and sheep. In: *Effects of poisonous plants on livestock*, Academic Press 229-237.
Pass, MA and Goosem MW (1983). Bile canalicular injury in lantana poisoning. *Toxicon*, **21**(3) 337-340.
Pour BM, Latha LY and Sasidharan S (2011). Cytotoxicity and oral acute toxicity studies of *Lantana camara* leaf extract. *Molecules*, **6**(5) 3663-74.
Blowey RW and Weaver AD (2011). *Color Atlas of Diseases and Disorders of Cattle*, 3rd Edn, Mosby Ltd.
Sebastian MM (2007). Role of pathology in diagnosis. In: *Veterinary Toxicology* Elsevier Ltd. 1100-1136.
Shafi TA, Siddiqui M, Sakhre MP, Syed AM, Borikar ST and Digraskar SU (2020). Successful treatment of *Lantana camara* poisoning in sheep. *EC Veterinary Science* **5**(2) 1-5.
Sharma OP, Makkar HP and Dawra RK. 1988. A review of the noxious plant *Lantana camara*. *Toxicon* **26**(11) 975-87.
Sharma OP, Sharma S, Pattabhi V, Mahato SB and Sharma PD (2007). A review of the hepatotoxic plant *Lantana camara*. *Critical Reviews in Toxicology*, **37**(4) 313-52.
Singh S (2018). Studies on clinico-haemato-biochemical changes and therapeutic management of Lantana toxicity in cattle. M.V.Sc. thesis submitted to College of Veterinary and Animal Science, Navania, Vallabhnagar, Udaipur (Rajasthan University of Veterinary and Animal Sciences, Bikaner (Rajasthan), India.
Srikanth K and Kumar KS (2013). Dermatitis due to Lantana toxicity and its management-a report of eight cattle. *Intas Polivet*, **14**(2) 218-220.
Stegelmeier BL, Field R, Panter KE, Hall JO, Welch KD, Pfister JA, Gardner DR, Lee S T, Colegate S, Davis TZ, Green BT and Cook D (2013). Selected poisonous plants affecting animal and human health. In: Haschek and Rousseaux's *Handbook of Toxicologic Pathology*, 3rd Edn. 1259-1314.
Tarunpreet and Saganpal (2021). Study on haemato-biochemical changes in Lantana toxicity affected cattle in southern Rajasthan. *Veterinary Practitioner*, **22**(1) 126-128.
Varga A and Puschner B (2012). Retrospective study of cattle poisonings in California: recognition, diagnosis and treatment. *Veterinary Medicine*, (Auckl) **3** 111-27.