

A REVIEW ON: *THEVETIA PERUVIANA*

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ABSTRACT

Thevetia peruviana are potentially lethal plants after ingestion. The plants is common toxicological emergency in tropical and subtropical parts of the world and international self-harm, using *T. peruviana* is prevalent in south Asian countries, especially in India and Sri Lanka. All parts of these plants are toxic, and contain a variety of cardiac glycosides including nerifolin, thevetin A, Thevetin B and oleandrin. Ingestion of oleander results in nausea, vomiting, abdominal pain, diarrhoea, dysrhythmias and hyperkalemia. In most cases; clinical management of poisoning by either *N. oleander* or *T. peruviana* involves administration of activated charcoal and supportive care. This article compiles all the information related to *Thevetia peruviana*.

Keywords: oleander poisoning, arrhythmias, cardiac glycosides, cannogenin. Pharmacological

INTRODUCTION

Medicinal plants as a group comprise approximately 8000 species and around 50% of all the higher flowering plant species of India. Millions of rural households use medicinal plants in a self-help mode. Half million practitioners of the Indian system of medicine in the oral and codified streams use medicinal plants in preventive, promotive and curative application. There are estimated to be over 7800 manufacturing units in India. In recent years, the growing demand for herbal product has led to a quantum jump in volume of plant metabolite previously with unknown pharmacological activities have been extensively investigated as a source of medicinal agents^{1,2}.

Description Of Plant

Figures of *Thevetia peruviana*:- (Fig 1 and 2)

Pharmacological Classification

Botanical Name : *Thevetia peruviana*
Family : Apocynaceae
Genus : *Thevetia*
Kingdom : Plantae
Order : Gentianales
Species : *T. peruviana*
Common Names : Kolke (Bengal), Mexican oleander, Yellow Oleander, Lucky Nut.³

Macroscopic Character

Taste: seed are very bitter, when chewed produce numbness

Colour: seed are green to greenish black

Odour: none

Shape: Oblong, hard

Distribution

This plant is native of Central & South America, but now frequently grown throughout the tropical and sub-tropical regions. It is an evergreen tropical shrub or small tree that bears yellow or orange-yellow, trumpet like flowers and its fruit is deep red/black in color encasing a large seed that bears some resemblance to a Chinese "lucky nut." It contains a milky sap containing a compound called Thevetin that is used as a heart stimulant but in its natural form is extremely poisonous, as are all parts of the plants, especially the seeds. Its leaves are long, lance shaped and green in colour. Leaves are covered in waxy coating to reduce water loss (typical of oleanders). Its stem is green turning silver/gray as it ages.⁴

CULTIVATION AND PROPAGATION

Cultivation

Thevetia peruviana is cultivated as an ornamental plant, and planted as large flowering shrub or small ornamental tree standards in gardens and parks in temperate climates. In frost prone areas it is container plant, in the winter season brought inside a greenhouse or as a house plant. It tolerates most soils and is drought tolerant. Exposure: part, full, or reflected sun; revels in heat Water: ample is best Soil: improved garden soil with good drainage Maintenance: low; periodic pruning and litter cleanup; training when young to tree if desired Can be grown as shrub or tree outside in warmer climates but in frost prone areas best brought back inside for winter. Will tolerate most kinds of soil as long as they are well drained and are situated in full sun in a sheltered area. Useful as a landscaping plant in warmer climates as it does not need much maintenance.⁵

Propagation

Propagate by seed in spring (clean seed coat in a glass containing 10% bleach 90% warm water for 2-3min; after wash seed and soak in warm water for 24h). Can also propagate from cuttings in spring-early summer with hardwood cuttings. For both use seed cutting compost that contains perlite.⁶

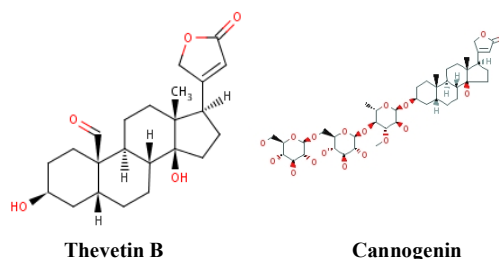
PARTS USED

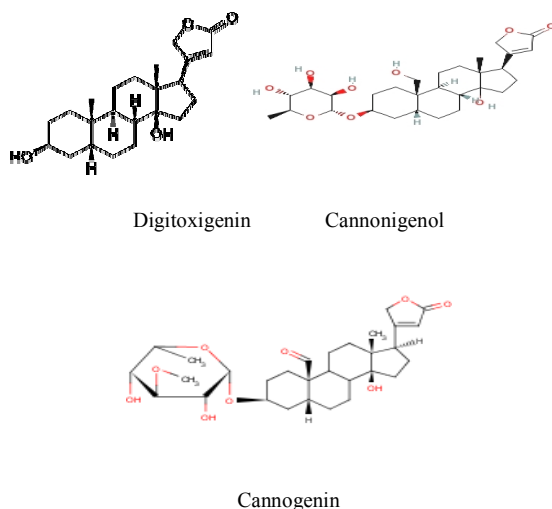
Thevetia peruviana is an ornamental plant, and mostly all parts of plants are medicinal use. These are Flowers and leaves, seed and root.

Table 1 Chemical Constituent

These are the chemical constituent which is present in the various parts of plants.

Structure Of Chemical Constituent





TOXIN

Thevetia peruviana plants are toxic to most vertebrates as they contain cardiac glycosides. Many cases of intentional and accidental poisoning of humans are known.⁷ The toxins are cardenolides called Thevetin A and Thevetin B (Cerebroside), others include Peruvidoside, Neriifolin, Thevetoxin and Ruvidoside. These cardenolides are not destroyed by drying or heating and they are very similar to digoxin from *Digitalis purpurea*. They produce gastric and cardio toxic effects. Antidotes for treatment include atropine and Digoxin antibodies and treatment may include oral administration of activate charcoal.^{8,9,10} Ovine polyclonal anti-digoxin Fab fragment antibody can be used to treat digoxin poisoning.¹¹

TOXICITY STUDIES

Study showed that raw *Thevetia* seed cake, even at a low 5% replacement of soybean

Meal in the diet is very toxic and lethal to rabbits. Death may have occurred because of thevetins A and B

And other multisystem effect of toxins. Tp seed cakes need adequate processing to remove toxic agents and

Anti-nutritive factors. Processing may allow it to be used as a protein supplement in rabbits and other live

Stock feeds.

BIOLOGICAL PEST CONTROL

The plants toxins have tested in experiments for uses in biological pest control. *Thevetia peruviana* seed oil was used to make a plant with antifungal, antibacterial and antitermite properties.¹² it is a plant toxin insecticide for termites. *Thevetia peruviana* inhibited spermatogenesis in rats, indicating the possibility of developing herbal male contraceptive.¹³

MEDICINAL USES

Thevetia peruviana contains a milky sap containing a compound called thevetin that is used as a heart stimulant but in its natural form is extremely poisonous, as are all parts of the plants, especially the seeds. The toxins are cardenolides called Thevetin A and Thevetin B (Cerebroside), others include peruvidoside, neriifolin, thevetoxin and ruvidoside. These cardenolides are not destroyed by drying or heating and they are very similar to digoxin from *Digitalis purpurea*. They produce gastric and cardio -toxic effects. Antidotes for treatment include atropine and Digoxin antibodies and treatment may include oral administration of activate charcoal. These toxins have also been experimented for use

in pest control. Entire *Thevetia* plant is very poisonous and the seeds are most poisonous. Tincture is cathartic emetic and febrile seeds are used as abortifacient and purgative in rheumatism and dropsy. Peruvidoside is used in treatment of mild cardiac insufficiency and weak heart. This drug shows relatively high degree of therapeutic index compared to digoxin.¹⁴

PHARMACOLOGICAL ACTIVITY

Antimicrobial activity

The antimicrobial activity of ethanol extract obtained from *Thevetia peruviana* was tested against bacterial species of *Escherichia coli*, *Streptococcus lactis*, *Enterobacter aerogenes*, *Alcaligenes faecalis* *Pseudomonas aeruginosa*, *Proteus vulgaris* and fungal species of *Fusarium oxysporum*, *Alternaria helianthii*, *Curvularia lunata*, *Aspergillus niger* and *Penicillium spp.* Better antimicrobial activity was observed with the extracts showed maximum activity against *E. coli*.¹⁵

Antifungal properties

Seeds of *Thevetia peruviana* were screened for their antifungal photo activity. Extracts obtained either with n-hexane or dichloromethane were fractionated by column chromatography or further analysed by thin-layer chromatography. All seed extracts and fractions were tested for inhibition of the fungus *Cladosporium cucumerinum* for the evaluation of photoactive inhibitory effects. Antifungal light-dependent activity was observed for some of the fractions and both crude extracts. The most photoactive fraction was analysed by capillary gas chromatography with mass spectrometry in order to identify its constituents.¹⁶

Piscicidal activity

The leaf and bark of *Thevetia peruviana* plant was administered for 24 h to the freshwater fish *Catla catla* (Hamilton) to evaluate their piscicidal activity in laboratory and cemented pond condition. The values of leaf and bark extracts of different solvents (i.e., acetone, diethyl ether, ethyl alcohol, chloroform and carbon tetrachloride) of this plant to fish *Catla catla* were determined. The LC50 values of acetone leaf extract of *Thevetia peruviana* plant is 88.80 mg/L (24h) in laboratory condition and 529.38 mg/L (24h) in cemented pond condition; acetone bark extract of this plant is 99.43 mg/L (24h) in laboratory condition and 591.78 mg/L (24h) in cemented pond condition against freshwater fish *Catla catla*. Similar trend was also observed in case of other solvent (i.e., diethyl ether, ethyl alcohol, chloroform and carbon tetrachloride) of leaf and bark extracts of *Thevetia peruviana* plant against freshwater fish *Catla catla* in laboratory and cemented pond conditions. The acetone leaf and bark extract of this plant was very effective in comparison to other solvent extract in both the conditions. So, the biochemical analysis is taken only acetone leaf and bark extract of *Thevetia peruviana* plant in laboratory condition.¹⁷

Antispermatic activity

This study was conducted to evaluate the antifertility potential of *Thevetia peruviana* in male albino rats with their phytochemical evaluations. Phytochemical examination showed that plant is rich in active constituents, i.e. α -amyrin acetate, lupeol acetate, α -amyrin, β -amyrin, lupeol and thevetigenin. T. peruviana stem bark methanol extract (TPMTE) administered orally to male rats at the dose level of 100 mg/rat/day did not cause any significant reduction in body weight, while the weight of reproductive organs

reduced significantly. A significant fall in the total protein and sialic acid content of the testes, epididymides, seminal vesicle and ventral prostate, as well as in the glycogen content of testes was also observed; however, cholesterol was increased significantly. TPMtE also caused a decline in spermatogenic elements, i.e. preleptotene and pachytene spermatocytes, secondary spermatocytes, round spermatids and mature Leydig cells. At this dose level Leydig cell nuclear diameter, seminiferous tubular diameter and Sertoli area were significantly reduced ($p < 0.001$). The reduction in sperm density and motility resulted in 18% residual fertility. In conclusion, *T. peruviana* inhibited spermatogenesis in rats, indicating the possibility of developing a herbal male contraceptive.¹⁸

Effect of *Thevetia peruviana* seeds extract on in vitro growth of four strains of *Phytophthora megakarya*

A study was carried out in Yaounde (Cameroon) to test the antifungal activity of extracts of *Thevetia peruviana* seeds. Crude extracts were obtained after successive maceration with hexane, ethyl acetate and methanol. Seed extracts were tested for inhibition of *P. megakarya*, a causal agent of black pod disease of *Theobroma cacao*. Four strains of *P. megakarya* were used. Antifungal tests were performed by using three concentrations (12.5, 25 and 50 $\mu\text{l ml}^{-1}$) of crude extracts. Seven days after incubation on pea agar medium, the results showed that the use of 50, 25 and 12.5 $\mu\text{l ml}^{-1}$ of crude extracts with ethyl acetate resulted in 100, 70 and 50% inhibition rates respectively on *P. megakarya*. Methanol extract on the BOYO, TA121 and TA123 strains led to total inhibition, while 37.5, 43.2 and 63.9 % inhibition rates were recorded for BOK11 strain at 12.5, 25 and 50 $\mu\text{l ml}^{-1}$ concentrations of the extract respectively. These results suggest that crude extracts from *T. peruviana* seeds are efficient biocide substances with antifungal activity.¹⁹

Anti-Inflammatory

Thevetia peruviana seeds contain glucosides of neriifolin, acetylneriifolin and therein. Seed oil distillates of *Thevetia peruviana* have been found to contain anti-bacterial activity. In the present work, the fresh flowers of *Thevetia peruviana* were subjected to phytochemical studies. The results of the study showed that the flowers contain quercetin, kaempferol and quercetin-7-o-galactoside. The structure of the isolated compound was characterized by UV, ^1H NMR and ^{13}C NMR spectra. The anti-inflammatory character of the isolated compound was tested by in vitro method and the results of the study revealed that the isolated compound showed a biphasic property.²⁰

Antidiarrhoeal And Antimicrobial

This study screened the antidiarrhoeal, antimicrobial and a cytotoxic effect of ethanol-extracted leaves of yellow oleander (*Thevetia peruviana*). The extract was tested against castor oil-induced diarrhoea in a model of albino rats and showed significant antidiarrhoeal activity ($P < 0.01$). Disc diffusion technique was used to test the in vitro antibacterial activities of the extract and exhibited poor antibacterial activities against both Gram positive and Gram negative bacteria (mainly *Bacillus* sp). Ethanol-extracted leaves of yellow oleander showed narrow zone of inhibition in the bacterial lawns of *Shigella flexneri*, *Salmonella typhi*, *Klebsiella* sp, *Staphylococcus aureus* and *Shigella sonnei*. Cytotoxicity was determined against brine shrimp nauplii and LC_{50} of the plant extract was determined as 627.21 $\mu\text{g/ml}$. The

wide range of LC_{50} value denotes the safety effect of the extract.²¹

Anti-termite

Thevetia peruviana (Pers.) K. Schum. seed oil was used to make a surface coating with antifungal, antibacterial and anti-termite properties. The paint exhibited inhibitory activity against *Escherichia coli*, *Staphylococcus aureus*, *Bacillus subtilis* and *Candida albicans* in a concentration dependent manner. The antibacterial activities were statistically significant ($p = 0.05$). The repellent action of paint against subterranean termites (*Microtermes* spp.) was significant ($p = 0.03$). From these results, it was concluded that the *Thevetia peruviana*-based oil paint was self-preserving against microbes and substantially protected wood from subterranean termite attack.²²

Flavanone and Flavanol Glycosides / Reverse Transcriptase Inhibition

Flavanone and flavanol glycosides from the leaves of *Thevetia peruviana* and their HIV-1 reverse transcriptase and HIV-1 integrase inhibitory activities: Two new flavanone glycosides and a new flavanol glycoside were isolated from the leaves of *T. peruviana* and were investigated for their inhibitory effects against HIV-1 reverse transcriptase and HIV-1 integrase.

Cardenolide Glycosides

Study isolated four cardenolide glycosides and four triterpenoid saponins. Cardenolide glycosides 1 and 2 showed significant reversal effect on TRAIL resistance in human gastric adenocarcinoma cells.

Properties and constituents

Seeds contain a toxic glucoside, thevetin. Seeds yield a fixed oil containing triloein 63%, tripalmitin and stearin, 37%. Thevetin has been classified with the digitaline group so activity on the heart muscle, blood pressure elevation, heart irregularities. It also causes increased intestinal peristalsis, increased salivation, and pupil contraction.

Properties

Bark is emetic, febrifuge, and antiperiodic. Leaves are cathartic. Milky juice is poisonous and vesicant.²³

CONCLUSION

It is quite evident from this review that *Thevetia peruviana* contains a number of phytoconstituents which reveals its uses for various therapeutic purposes. Looking upon wide prospects and potential of Peruvian a for various purposes, This will help in financial upliftment of the poor and landless farmers besides providing base for the Research and Development. The Plant or its individual parts can be used for the treatment of various disorders in human being such as, diabetes, liver toxicity, fungal infection, microbial infection, inflammation, pyrexia and to relieve pain. Still, so much work is required with the thevetia to investigate the mechanism of actions with other therapeutic activities.

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REFERENCES

1. Bandara A, Scott A and Weinstein, Julian White and Michael Eddleston : A review of the natural history, toxicology, diagnosis and clinical management of *Nerium oleander* and *Thevetia peruviana* poisoning, Toxicology official journal of the International Society on Toxicology (2010) Volume 56, Issue 3, 1 September 2010, Pages 273-281

2. Patil R.K, Makari H.K and Gurumurthy H: in vitro antimicrobial activity of ethanol extract of *Thevetia peruviana*, ejaefche ISSN: 1579-4377
3. Kokate CK, Purohit AP and Gokhle SB: Pharmacognosy, Nirali Prakashan, Thirty Second Edition 2005, pp.201
4. Sastri BN (chief editor) .Wealth of India *Thevetia peruviana* (vol.1) New Delhi National Institute of Science Communication CSIR, P.218
5. <http://www.mobot.org/gardeninghelp/plantfinder/Plant.asp?code=A551> Kemper Center: Plant's Culture and Characteristics
6. http://ag.arizona.edu/pima/gardening/aridplants/Thevetia_peruviana.htm
7. Shannon D, Langford & Paul J. Boor (1996). "Oleander toxicity: an examination of human and animal toxic exposures". *Toxicology* 109 (1): 1–13. Doi:10.1016/0300-483X(95)03296-R. PMID 8619248.
8. Rajapakse S., Management of yellow oleander poisoning *Clinical Toxicology* 2009 47:3 (206-212)
9. Roberts D.M, Southcott E and Potter J.M, Roberts, Buckley N.A.: "Pharmacokinetics of digoxin cross-reacting substances in patients with acute yellow oleander (*Thevetia peruviana*) poisoning, including the effect of activated charcoal" *Therapeutic Drug Monitoring* 2006 28:6 (784-792)
10. Bandara V, Weinstein S.A and White J., Eddleston M.: "A review of the natural history, toxicology, diagnosis and clinical management of Nerium oleander (common oleander) and *Thevetia peruviana* (yellow oleander) poisoning" *Toxicon* 2010 56:3 (273-281)
11. Eddleston.M, S. Rajapakse and Rajakanthan, S. Jayalath, L. Sjöström and W. Santharaj et al. Anti-digoxin Fab fragments in cardio toxicity induced by ingestion of yellow oleander: a randomized controlled trial, *Lancet* 355 (2000), pp. 967–972.
12. Kareru P.G, Keriko J.M and Kenji G.M, Gachanja A.N: "Anti-termite and antimicrobial properties of paint made from *Thevetia peruviana* (Pers.) Schum. Oil extract" *African Journal of Pharmacy and Pharmacology* 2010 4:2 (087-089)
13. Gupta R, Kachhawa JB and Gupta RS, Sharma AK, Sharma MC, Dobhal MP: "Photochemical evaluation and antispermato-genic activity of *Thevetia peruviana* methanol extract in male albino rats." *Hum Fert (Camb)*. 2011 Mar; 14(1):53-9
14. http://en.wikipedia.org/wiki/Thevetia_peruviana
15. H.S.Ravikumar, Patil T.R and Kekuda P H.Gurumurthy: *In Vitro Antimicrobial Activity of Ethanol Extract Of Thevetia peruviana*. Vol. 2, Issue 1, 2008
16. Gata-Gonçalves, Nogueira F, and Olivia Matos, Raúl Bruno de Sousa Photoactive extracts from *Thevetia peruviana* with antifungal properties against *Cladosporium cucumerinum* *Ligia* Volume 70, Issue 1, April 2003, Pages 51-54
17. Singh SK, Yadav RP and Singh .A: Piscicidal activity of leaf and bark extract of *Thevetia peruviana* plant and their biochemical stress response on fish metabolism. 2010 Nov; 14(11):915-23.
18. Gupta R, Kachhawa JB and Gupta RS, Sharma AK, Sharma MC, Dobhal MP Photochemical evaluation and antispermato-genic activity of *Thevetia peruviana* methanol extract in male albino rats. 2011 Mar; 14(1):53-9.
19. Ambang Z, J Ngho Doohand and G. Essono, N. Bekolo, G. Chewachongl, Effect of *Thevetia peruviana* seeds extract on *in vitro* growth of four strains of *Phytophthora megakarya* C.C. *POJ* 3(3):70-76 (2010) ISSN:1836-3644
20. R. thilagavathi, helen P. kavitha and B. R. venkatraman: Isolation, Characterization and Anti-Inflammatory Property of *Thevetia peruviana* ISSN: 0973-4945; CODEN ECJHAO E-Journal of Chemistry 2010, 7(4), 1584-1590
21. M.M. Hassan, A.K. and Saha, S.A. Khan1, A. Islam, M. Mahabub-Uz-Zaman2 and S.S.U. Ahmed3 : Studies on the antidiarrhoeal, antimicrobial and cytotoxic activities of ethanol-extracted leaves of yellow oleander (*Thevetia peruviana*) *Open Veterinary Journal*, (2011), Vol. 1: 28-31 ISSN: 2218-6050
22. P. G. Kareru, J. M. Keriko, G. M. Kenji and A. N. Gachanja: Anti-termite and antimicrobial properties of paint made from *Thevetia peruviana* (Pers.) Schum. Oil extract *African Journal of Pharmacy and Pharmacology* Vol. 4(2). pp. 087-089, February, 2010 ajpp ISSN 1996-0816 © 2010 Academic Journals
23. <http://www.stuartxchange.org/index.html>



Fig 1



Fig 2

Table 1 CHEMICAL CONSTITUENT

These are the chemical constituent which is present in the various parts of plants

Glycoside	Aglycone	Sugars
Cereberoside (Thevetin B)	Digitoxigenin	L-thevetose+2mol.D-glucose
Thevetin A	Cannogenin	L-thevetose+2mol.D-glucose
Peruvoside	Cannogenol	L-thevetose
Neriifolin	Digitoxigenin	L-thevetose
Thevenerin	Cannogenol	L-thevetose
Peruvosidic acid	Cannogenic acid	L-thevetose