REVIEW ARTICLE

Thevetia peruviana: Its Phytochemistry, Traditional and Medicinal Uses, and Pharmacological Activities

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Received: 08th October, 2023; Revised: 26th October, 2023; Accepted: 13th November, 2023; Available Online: 25th December, 2023

ABSTRACT

Thevetia peruviana, a member of the Apocynaceae family, is also known as digoxin, fortunate nut, yellow oleander, and other names. After consumption, *T. peruviana* plants have the potential to be fatal. In South Asian countries, especially in Sri Lanka and India, *T. peruviana* is frequently used for international self-harm. Around the world's tropical and subtropical regions, *T. peruviana* is a common cause of toxicological emergencies. The entire plant is hazardous due to the presence of several cardiac glycosides, including neriifolin, oleandrin, thevetin A, and thevetin B. Oleander consumption causes hyperkalemia, vomiting, diarrhea, abdominal pain, and all of the above. In the majority of cases, supportive care and the administration of activated charcoal are used in the clinical therapy of either *N. oleander* or *T. peruviana* poisoning. *T. peruviana*-related information is compiled in this article.

Keywords: *Thevetia peruviana*, Magnoliopsida, Pharmacological activities, Juveno-mimetic activity, Anti-termite activity.

International Journal of Drug Delivery Technology (2023); DOI: 10.25258/ijddt.13.4.81

How to cite this article: Chauhan VS, Mazumder A, Chandel S. *Thevetia peruviana*: Its Phytochemistry, Traditional and Medicinal Uses, and Pharmacological Activities. International Journal of Drug Delivery Technology. 2023;13(4):1657-1663.

Source of support: Nil.

Conflict of interest: None

INTRODUCTION

It is concluded from the literature review that there is a lack of exhaustive knowledge from science on *Thevetia peruviana*, and the information gathered may be applied as a supplementary source for upcoming research into the physiological and anatomical properties of plants, the development of preparations, the writing of publications, and as a support for the potential therapy of a variety of ailments.

T. peruviana belongs to the family of little ornamental shrubs known as Apocynaceae. Because of its yellow blossoms, it also goes by the names yellow oleander and pilli kaner, and it occurs all over India.[1]

Other names for it include Kaner, fortunate nut, milk bush, and yellow oleander. The world's tropical and subtropical forests are home to this evergreen plant.[2]

Depending on the amount of rainfall and plant age, they can produce 400–800 fruits each year when grown as hedges. The usually green, round fruits eventually turn black as they develop. A fruit has a seed and can have 1-4 seeds in its shell when it is divided horizontally and diagonally.

All of these plants' organs contain milky liquid, and they are dangerous because they contain cardiac glycosides that were studied like neriifolin and Peruvoside.[3]

The fruit has a milky fluid within that includes thevetin, a cardiac stimulant. All plant parts, especially seeds, are extremely harmful in their unaltered states.

T. peruviana is a large flowering bush that can grow in a variety of soil types and can survive dry conditions. Figure 1 depicts the plant's yellow-colored flowers, lance-shaped leaves, and massive green seeds (Figure 1). In warmer climates, it can be increased in size externally as a woody plant or tree if desired. These plants can survive a wide range of soil types in so far as they remain in direct sunlight, in a protected location, and well-drained. Since it may be used as an ornamental plant and needs little upkeep, it is excellent in warmer climates.[4]

Taxonomical classification
Kingdom: Plantae
Subkingdom: Tracheobionta
Super division: Spermatophyta
Division: Magnoliophyta
Class: Magnoliopsida
Subclass: Asteridae

Figure 1: Illustration of plant part

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Order: Gentian ales
Family: Apocynaceae
Genus: *Thevetia*
Species: *peruviana*

Habitat

In dry regions with severe drought, gardens use the sides of roads as soil binders.

Distribution

Despite being a native of South and Central America, this plant is now frequently grown in tropical and subtropical regions. This evergreen tropical shrub or tree produces small, trumpet-shaped, yellow or orange-yellow flowers. The fruit is dark red or blackish in color and contains a large nut that resembles a Chinese "lucky nut" in some ways. It has a milky secretion that is exceedingly deadly in its natural state, just like all plants, particularly the seeds, and is employed as a heart stimulant.

Its leaves are enormous and long, orbicular, and greenish in color. Oleanders typically have waxy coatings on their leaves to prevent water loss. As it ages, the stem's green color turns silvery or grey.[5]

Description of the Plant

Thevetia peruviana belongs to the Apocynaceae family, sometimes called as digoxin, fortunate nuts, yellow oleander, and other names. Although it is originally from Mexico, South and Central America, this plant is now a tropical, evergreen decorative tree or bush that can reach heights of up to 10 to 15 feet. Plant is oedema-curing, diuretic, and cardiotonic. The leaves are lance-shaped, green, and spirally organized. They are linear, measuring 13 to 15 cm in length. The waxy coating is applied to the leaf surface to prevent water loss. A huge seed that resembles a Chinese "lucky nut" is enclosedin a deep crimson or black fruit with a yellow, trumpet-like blossom as demonstrated in Figure 2. A huge seed that resembles a Chinese "lucky nut" is enclosed in a deep crimson or black fruit with a yellow, trumpet-like blossom. As it ages, the stem turns from green to silver or grey. Tumors are treated with root paste applied as plaster. The plant grows in locations with various types of well-irrigated soils and in shaded areas.

Thevetia is the scientific name given to the plant by French missionary Andre Thevt (1502–1590), who gathered species in South America. The yellow oleander has poisonous sap and seeds. The seeds have a cardiac stimulant in them. It provides oil for Chinese industry and can thrive in tough weather conditions, making it useful for restoring degraded soil.

Figure 2: Seeds of *Thevetia peruviana*

Thevetia cake contains 48% protein content with fat extraction, but Atteh (1995). According,[6] it is dangerous for broilers and needs to be processed further before it can be utilised efficiently as a part of animal feed.

T. peruviana, also called *Nerium oleander*, and yellow oleander, often known as common oleander, are two plant species that flourish in temperate areas worldwide. Both species include substances known as "cardiac glycosides," which have effects comparable to those of the digoxin heart medication. According to numerous accounts, both species can be harmful when consumed orally and can even result in human mortality.[7] Additionally, this plant has the potential to synthesize cardiac glycosides, like neriifolin and peruvoside, having a higher therapeutic index than digoxin. Furthermore, there is a dearth of knowledge about the antifungal activities of yellow oleander in plant protection in several African countries.[8-20]

Traditional uses

T. peruviana bark has historically been used for amenorrhea, intermittent fever, ulcers, febrifuge, purgative, and snake bites. The leaves are used to treat jaundice, fever, intestinal worms, and to treat violent headaches and colds. The seeds are used as an abortifacient, an emetic, to treat hemorrhoids skin ailments, and to treat rheumatism.

Cultivation and Propagation

Cultivation

In parks and gardens in temperate climates, *T. peruviana* is grown for ornamental purposes and planted as a sizable blooming shrub or as a tiny ornamental trees. It is a pot plant that can be utilized as a garden plant during the winter in freeze-thaw areas or transported inside a nursery. It can withstand drought and most types of soil. Exposure: basks in reflected or part sun; loves heat. Ample water is excellent. Enhanced garden soil with excellent drainage low maintenance; occasional trimming and litter removal; optional training of young trees in warmer climes, it is possible to grow this outside as a shrub or tree, but it is recommended to bring it inside for the winter in frost-prone places.[21]

Propagation

In the spring, sow seeds and let them soak in hot water for 24 hours after cleaning the seed coat in a glass with 10% bleach and 90% hot water for 2-3 minutes. It can also be grown in the early stages of summer or spring from cuttings of hardwood.[22]

Pharmacological Activities of this Plant

Anti-diarrhoeal activity and Antimicrobial activity

The yellow oleander leaves' antidiarrheal, antibacterial, and cytotoxic effects were examined in this study (*T. peruviana*). In a model of albino rats exposed to castor oil-induced diarrhea, the extract was examined and showed considerable antidiarrheal action (P 0.01). Using the disc diffusion technique, the extract's *in-vitro* antibacterial activity was evaluated, and it was discovered that it was not effective to gram positive as well as gram negative bacteria (especially *Bacillus* species).

Shigella flexineri, Shigella sonnei, *Klebsiella* sp., the bacteria *Staphylococcus aureus*, and *Salmonella typhi*'s bacterial lawns were all inhibited by a decoction of yellow oleander leaves made with ethanol.

The cytotoxicity of the plant extract was examined in shrimp from brine nauplii, and the value of the LC_{50} was determined to be 627.21 g/mL.

The broad range of the LC50 value indicates the extract's safety effect.[23]

Antibacterial activity

The antibacterial capabilities of the extract, which typically failed to kill Bacillus species, were emphasized by Hassan and colleagues.

Yellow oleander exposed to ethanol showed a narrow area of antagonize in tests against a microbial colony of the bacteria *Shigella flexineri, Syphilis typhi, S. aureus*, other *Klebsiella* species, and *Shigella sonnei.*

Using saline prawns' organisms to test the herbal extract's cytotoxicity, its LC_{50} value was discovered to be 627.21 g/mL. The extensive LC50 range suggests that the extract has protective properties. The extracts of *peruviana* prepared with methanol have been shown to have a significant antioxidant activity when several plant components' anti-oxidant and antibacterial properties were examined using aqueous and ethanol crude extracts.

Using an agar well diffusion test (*Candida albicans*), Alisha and her team assessed the antibacterial properties of *T. peruviana* material against the bacteria *E. coli, Pseudomonas anginose, Bacillus subtilis, Staphylococcus aureus*, filamentous black fungus (*Micro coccinellid's*), and unicellular fungus.[24-28]

Anticancer activity

Alberto Ramos-Silva and team employed the MTT assay to assess the potential anticancer properties of the *T. peruviana* fruit methanolic extract.

The extraction dramatically decreased cell motility and engraftment in all examined cancer cell lines.[29] Aisha and colleagues investigated the potential to fight cancer of *T. peruviana* latex-based against prostatic cancer cell (PC3) and cancer of the mammary cell (MCF7) using the MTT technique (MCF7). They found that PT had a 1000 g/mL concentration with an IC_{50} of 48.26 g/mL for PC3 poisoning and 40.31 g/mL for MCF7 damage, respectively.

Unquestionably, recent research has demonstrated that latex contains numerous substances that are very useful in the fight against cancer.[30,31]

Anticoagulant activity

Researchers utilized PT time and powered incomplete thromboplastin time assays to assess the cell viability anti-coagulation action of PT mucilage, and it was discovered that it possesses effective anticoagulant properties.[32-35]

Antifungal activity

T. peruviana seedlings were examined for antifungal photoactivity. Thin-layer chromatography was employed for further examination, and column chromatography has been used to separate decoction prepared using dichloromethane or n-hexane. *Cladosporium cucumerinum* was assessed for suppression by all seed and fractional extracts to investigate photoactive inhibitory characteristics. Some of the fractions and both extracts showed antifungal light-dependent activity.[36]

Anti-haemolysis activity

Aisha and crew looked at erythrocyte membrane stability as a way to gauge a substance's ability to lower inflammation. Using this strategy resulted in cell lysis because the current investigation was conducted in a hypotonic environment. However, it wasn't until a maximum latex level of 1000 g/ml that the haemolysis inhibition percentage reached 58.5%.

One or more natural substances that are present in latex may hinder hemolysis. At 200 g/ml of indomethacin, which was utilised to test the efficacy of latex, the maximal hemolysis inhibition was found to be obtained at 91%. Anti-inflammatory effects of *T. peruviana* and calotropisprocera latex have been demonstrated.[37,38]

Anti-spermatogenic activity

This study examined *T. peruviana* 's potential to prevent infertility in male normal rats and its phytochemical composition. Table 1 narrates the phytochemical constituents s of the herb. A phytochemical analysis discloses that the herb is rich in bioactive ingredient, including lupeol, *Thevetigenin*, l-amyrin, and l-amyrin acetate. Male rats were given 100 mg/rat/day of *T. peruviana* bark methanolic extract by oral route, and while the weight of the reproductive organs dramatically decreased, the weight of the body did not significantly decrease.

The total protein, sialic acid, seminal vesicle, ventral prostate, glycogen, and the content of sialic acid in the testes, ventral prostate, and epididymis all dramatically decreased, whereas cholesterol significantly rose. The spermatogenic components, such as mature Leydig cells, secondary spermatocytes, round spermatids, and preleptotene and pachytene spermatocytes, decreased as a result of TPMtE. The nuclear diameter of Leydig cell, the seminiferous tubular, and the Sertoli portion all saw substantial reductions at this dose level (p 0.001). 18% of fertility was still present despite the decrease in sperm density and motility.

In conclusion, the fact that *T. peruviana* suppressed the formation of sperms in rats suggests the potential for creating a natural male contraceptive.[39]

Anti-diabetic activity

Tests on *T. peruviana* bark for its in vivo anti-diabetic impact in streptozocin (Streptozocin)-induced diabetic rats indicated substantial efficacy in a dose-dependent manner, which was the main goal of Tabrez *et al.*'s research.[40]

Anti-tum our activity

According to Tabrez *et al.* study's EAC cell line was successfully treated in experimental animals using methanol extracts of *T. peruviana* fruit.

The EAC control group's tumor volume, viable cell count, and tumor weight were all higher than those in the extract-treated group. The tumor volumes were 3.62 0.12, 2.88 0.23,

and 1.34 0.17 mL for the extract-treated groups (50 mg/kg and 100 mg/kg body weight), respectively.

The extract notably ($p < 0.001$) reduced the peroxidation of lipids in contrast to the EAC control group and returned decreased catalase, superoxide dismutase, and glutathione to their pre-reduction levels.[41]

Larvicidal activity

The effectiveness of *T. peruviana* leaves extract in methanol was tested against *A. aegypti* larval stages. In comparison to pupae and larval stages, the IV instar of *A. aegypti* larvae in this study displayed less vulnerability. Increased mortality was a result of concentrations, and the larvae also gradually developed melanisation.[42]

T. peruviana leaf extracts were used to test the plant's potency against the *Aedes aegypti*, *Anopheles stephensi*, and dengue mosquito larvae that transmit malaria. After 24 hours, it was discovered that the mean LC_{50} values for the leaf extracts of *T. peruviana* in C3H6O, petroleum-based ether, CHCl3, and methanol were 0.045, >0.05, 0.026, 0041, and 0.038, >0.05, 0.021, and 0.036%, respectively.

The delayed effect of chloroform extract after three days demonstrated that the inhibition of insect growth probably brings about larvicidal activity.[43]

Juveno-mimetic activity

As a significant pest of cotton and okra, the red thread bug, *Dsydercus cingulated*, fresh *T. nerifolia* seeds and leaves were investigated by Bai H. and colleagues for their ability to operate as juvenomimetic agents. 40% leaf and 10% seed extracts showed noticeable activity in terms of larval death from the disease, the span of the ovipositional duration, the growth of deformed adults, and diminished fecundity of the bugs. The 20 leaf and 5% seed extract treatments had noteworthy impacts, in contrast with the 10% leaf and 2.5% seed extract treatments' lack of effects.[44]

Gastro-protective activity

Pragati and company focused on the gastro-therapeutic properties of *T. peruviana* and found that it had such activity using indomethacin- and ethanol-induced gastric lesions as their models.[45]

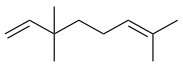
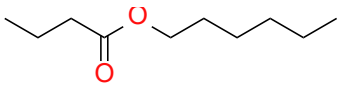
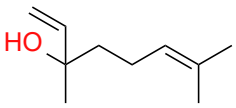
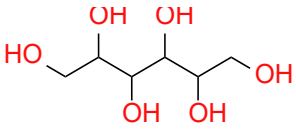
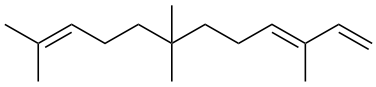
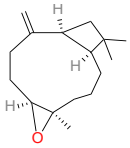
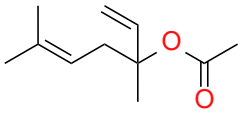
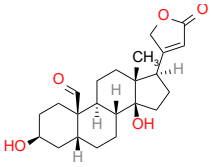
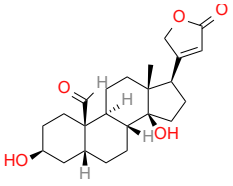
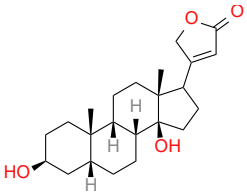
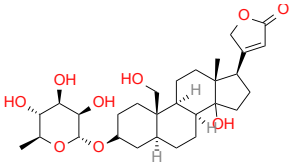
Locomotor activity

Pragati and her team investigated the locomotor behavior of *T. peruviana*. In contrast to mice receiving a control (2012 497 counts in 90 minutes), locomotor activity was observed in mice following either oral administration of treatment oil at a concentration of 100 mg/kg or breathing the substance for 60 minutes.[45]

Piscicidal activity

To measure the piscicidal's efficacy in a lab setting and in a concrete pond, leaf and trunk from the *T. peruviana* plant were administered for 24 hours. Using a variety of solvents (C3H6O, DEA, ethylene glycol, CHCl3, and CCl4), the impact of this plant's leaflet and stalk extracts on the fish Catla catla were evaluated. The LC_{50} values of the acetone leaf and extracts

Table 1: Chemical constituents present in plant

Camphene	
Ocimene	
Hexyl butanoate	
Linalool	
D- glucitol	
Faenesene	
Caryophyllene oxide	
Linalyl acetate	
Thevetin b	
Cannogenin	
Digitoxigenin	
Cannonigenol	

of bark of *T. peruviana* in the research setting are 88.80 and 99.43 mg/L, respectively.[46]

Cytotoxic activity

Hassan and others used an experiment involving brine shrimp lethality to test the cell damage activity of *T. nerifolia* leaf extract. At six multiple doses of the extracts of *T. peruviana* leaves, dose-related mortality in the percentage fatality of Artemia salina was seen. At doses like 62.5, 125, 250, 500, 1000, and 2000 g/mL, death rates of 0, 5, 10, 35, 65, and 100% were observed.[47]

Anti-termite activity

A surface coating with anti-termite, antibacterial, and antifungal characteristics was created using the seed oil of *Thevetia peruviana*. In a dose-related manner, the paint displayed inhibitory capability against various bacterial species ($p<0.05$). The antibacterial activity was statistically significant. The paint substantially repelled underground termites (Micro Termes spp.; $p < 0.03$). The oil surface made from *T. peruviana* was discovered to be self-preserving towards microbes.[48]

Antimicrobial activity

Thevetia peruviana's ethanol extract was tested for its ability to fight off the bacteria*, Enterobacter aerogenes, Escherichia coli, Alcaligenes faecalis, Pseudomonas aeruginosa, Streptococcus lactis* and *Proteus vulgaris* as well as the fungi *Curvularia lunata, Fusarium oxysporum, Alternaria helianthin*. The extracts' greatest antibacterial effectiveness against *E. coli* was associated with better antimicrobial activity.[49]

Medicinal Uses of *T. peruviana*

T. peruviana is a plant that produces a milky ebonite that includes thevetin, used as a cardiac booster but is also exceedingly deadly in its natural state. Cardenolides termed Thevetin A and Thevetin B (Cerebroside) are among the toxins; another includes Ruvoside, Thevetoxin, neriifolin, and Peruvoside. These cardenolides are remarkably comparable to the digoxin from Digitalis purpurea and are not damaged by drying or boiling. They have harmful effects on the heart and the stomach. Digoxin and Atropine antibodies are used as therapeutic antidotes, and activated charcoal may also be administered orally. Additionally, these poisons have been tested for use in insect control. Entire The seeds of the thevetin plant are particularly toxic. Febiuge seeds are used as a purgative for arthritis and dropsy, and the tincture is an emetic with cathartic properties. Peruvoside is used to treat weak hearts and moderate cardiac insufficiency. Compared to digoxin, this medication exhibits a comparatively high level of therapeutic index.[50]

CONCLUSION

Currently, the majority of the human population uses herbal treatments to treat ailments, and they prefer herbal drugs merely due to their fewer negative effects. Despite being a beautiful decorative plant with a lot of pharmacological action, *T. peruviana* has been identified as harmless at various levels of research. According to the plant's pharmacognostic traits, HPLC testing, and gas chromatography, *T. peruviana* is an excellent source of vitamin B6, K, and Ca required to cure different conditions, such as being overweight, digestive problems and inflammatory diseases. Due to the plant's significant properties, which form the basis of several research areas, rigorous sociological research is necessary.

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