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# KARAVEERA IN THE LIGHT OF AGADATANTRA (TOXICOLOGY) – A REVIEW ARTICLE

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## ABSTRACT

Karaveera, although considered an Upaviṣa (Potentially toxic substance), has been a part of Ayurvedic medicine for treating various diseases. The different parts of Karaveera and its various dosage forms have been employed in both external and internal applications to address numerous health conditions. Pita Karaveera (Thevetia peruviana) is a medicinal plant known for its wide range of pharmacological properties, but it has not received significant scientific attention. Classical texts on Ayurveda were written over different periods since the field's inception. Unfortunately, this information has not been critically reviewed or published in a comprehensive format. Therefore, a systematic review concerning the identification and use of this classical drug is essential. The plant contains active compounds like cardiac glycosides, particularly peruvoside, which have been well-studied. Its bark tincture is used for malarial fever and snakebites, while macerated leaves and bark treat amenorrhea. A decoction of leaves helps with jaundice, fever, and intestinal worms. Karaveera is classified in classical Ayurveda by its synonyms, varieties, group, tastes, actions, and therapeutic uses, primarily for treating Kuṣṭha (Leprosy). More research is essential to explore its medicinal value for mankind. Suicide is common amongst village women, the use of it as a paste or decoction. So, it is also important in forensic medicine.

**KEYWORDS:** Ashvamara, External uses, Internal uses, Nerium oleander, Poisons, Thevetia peruviana, Upaviṣ, Medico-legal, Toxic, Postmortem.

## INTRODUCTION

Pita Karaveera **(**Thevetia peruviana) is a medicinal plant with a wide array of pharmacological properties, but yet not received considerable scientific attention. The plant belongs to the family Apocynaceae and is commonly known as yellow oleander. The plant is native to Central and South America, especially Mexico, Brazil, and West Indies but is now frequently cultivated throughout the tropical land including countries like India and Sri Lanka as an ornamental plant and holy plant whose flower is used in the worship of lord Shiva.[1]

### Taxonomical classification[2]

Kingdom: Plantae

Subkingdom: Tracheobionta

Superdivision: Spermatophyta

Division: Magnoliophyta

Class: Magnoliopsida

Subclass: Asteridae

Order: Gentianales

Family: Apocynaceae

Genus: Thevetia

Species: peruviana

### Synonyms[3]

Important Synonyms (Vernacular name) Attributed to *Karavira*

Hindi: *Peeli, Kaner, Kulkephul, Karavira*

Sanskrit: *Divyapushpa, Pita-Karavira, Ashvaghna*

Telugu: *Pachaganneru, Kastooripatte*

Tamil: *Thiruvachipoo, Ponnarali Pachaiyalari, Sivappu, Sevvarali, Aatrulari*

Kannada: *Kadukasi, Kanagile, Kharjahar*

Malayalam: *Manjaarali, Kanaveeram*

Assamese: *Diflee, Sammulhimar*

Manipuri: *Utonglei*

Bengali: *Kolkaphul*

Marathi: *Bitti*

Manipuri: *Utonglei* etc.

**Morphological description**[4]

Thevetia peruviana is an evergreen shrub or small tree normally approximately 3-8m tall.

**Leaves**-The leaves are in pairs or whorls of three, thick and leathery, darkish-green, slender lanceolate, 5– 21 cm (2.0–8.3 in) long, and 1–3.5 cm (0.39–1.4 in) wide, and with a whole margin**.**

**Flowers: -** Flowers are shiny yellow and funnel-shaped with spirally twisted. They develop in clusters at the end of every new branch. The flower may be 2.5–5 cm (0.98–2.0 in) in diameter, with a deeply 5-lobed fringed corolla around the central tube in a manner that looks like a funnel tube. They are regularly, but not constantly, sweet-scented.

The fruits are somewhat globular, slightly fleshy, and have a diameter of 4-5cm. The fruits, which are green in colour, become black on ripening. Each fruit contains a nut, which is longitudinally and transversely divided. All parts of the plant contain the milky juice.

**Root bark**

**Acc. to *ayurveda***

करवीरववषे तापो कोष्ठेभववत दारुण:| स शूलौ ववततरेकौ च भवेदाक्षेपको गद: || (Anupana Manjaree)

**Types of *karavira* in various *nighantus***

*Shveta* (White), *Rakta* (Red): - *Dhanvantari nighaṇṭu,*[5] *Abhidhana Manjari*[6] *Bhavaprakasha Nighaṇṭu*[7] *Nighaṇṭusheṣa,*[8] *Madanpala Nighaṇṭu,*[9] *Sarasvati Nighaṇṭu,*[10] *Shodhala Nighaṇṭu,*[11] *Paryayaratnamala,*[12] *Candra Nighaṇṭu.*[13]

*Shveta* (White), *Rakta* (Red), *Pita* (Yellow): - *Kaideva Nighaṇṭu,*[14] *Shivakoṣa,*[15] *Priya Nighaṇṭu,*[16] *Nighaṇṭu Adarsha.*[17]

*Shveta* (White), *Rakta* (Red), *Pita* (Yellow), *Kṛiṣṇa* (Black): - *Raja Nighaṇṭu.*[18]

*Shveta* (White), *Rakta* (Red), *Gulabi* (Pink), *Pita* (Yellow), *Kṛiṣṇa* (Black): - *Shaligrama Nighaṇṭu.*[19]

**Ayurvedic properties: -*Gana***

Acc. To charak Samhita: *Tiktaskandha, Kusthaghna*

Acc. To Sushruta Samhita: *Laksadi, Shirovirechana* Raspanchak *(*Pharmacodynamics*)*

***Rasa****-Katu*[5, 14,17,19,20] *Tikta,*[5,7,14,19,20] *Kashaya*[17,13,14,19]

***Guna****- Laghu,*[13, 19,21] *Tiksna.*[17,19]

***Virya****- Usna*[5,7, 14,17,20,21]

***Vipaka****- Katu.*[7,20]

***Dosakarma****- Kaphavatasam*[20] **Karma**[5,7,9,13,14,17,19,20,21,22]**-** *Hrudya, Raktasodhaka, Svasaghna, Svedajanana, Jvaraghna, Visamajvarapratibandhaka, Vranasodhana-Ropana, Sothahara, Dipan, Vidahi, Bhedana. Vrana-dustvrana-nadivrana, Palitya, Indralupta, Upadansa-phirang, Ashmari-sarkara, Netrabhisyanda-netrakopa, Hrudroga-raktavikara, Svasarog, Udararoga-agnimandya-vibandha, Jvaravisamajvara, Tvakdosha, Ksudraroga, Kandu-pamakikkisa-kacchu, Bhagandar, Kusthaghna, Kandughna and Vishaghna.*

**Toxicity:** All components of the plant produce exceptionally poisonous latex; the kernels are the most poisonous. The active standards are cardiac glycosides of the cardenolide type; signs and symptoms of poisoning especially involve the cardiovascular system (Which includes the varieties of arrhythmias) and the gastrointestinal tract of the body. Vomiting is a protective mechanism of the body against any type of poisoning and hence it becomes a common symptom of poisoning. Ischemic modifications arise, in addition to palpitations. The most critical and instant reason leading to loss of life is peripheral vascular failure. The seeds were used for committing suicide, homicide, and as a tribulation poison. The absorption of the equivalent of two Thevetia peruviana leaves may be enough to kill a 12.5kg baby.[23]

**Pharmacological activities as per different research articles[24]**

**Antimicrobial activity: -**The antimicrobial activity of *Pita Karavira* (Thevetia peruviana) leaves extract with 95% alcohol as organic solvent turned into analysis in opposition to ten medically essential pathogenic microbes. The leaf extract of *Pita Karavira* proved to be powerful in opposition to Escherichia coli, Klebsiella pneumoniae, and Pseudomonas aeruginosa while Proteus Vulgaris confirmed susceptibility most effective if it is used in high doses. The extract was additionally confirmed as having moderate anti-microbial activity in opposition to Staphylococcus aureus, Candida albicans, Aspergillus Niger, Mucor, Rhizopus, and Penicillium species.[25] Thevetia peruviana seed oil is used to make a surface coating. The

*Pita Karavira* exhibited inhibitory activity in opposition to Escherichia coli, Staphylococcus aureus, Bacillus subtilis, and Candida albicans in a concentration-based manner.[26] The antimicrobial activity of ethanol leaf extract was examined in opposition to Escherichia coli, Salmonella typhi, Vibrio cholera, Shigella, and Staphylococcus aureus. The extract confirmed significant activity in opposition to E. coli and Shigella.[27] The antimicrobial capability of the experimental plant leaf extracts in comparison with callus extract is evaluated. A number of the gram-negative microorganisms the Pseudomonas aeruginosa appeared to be sensitive in opposition to all concentrations of *Pita Karaveera* leaf and callus extracts, even as Escherichia coli showed resistance with all concentrations of extracts. Callus extract of the *Pita Karaveera* possesses higher activity in assessment with leaf extract in opposition to gram-positive (Staphylococcus aureus and Bacillus cereus) and gram-negative (Pseudomonas aeruginosa) strains.[28] The antimicrobial activity of seed kernel extracts become Analysed in opposition to human skin pathogenic microbes. Antimicrobial efficacy in opposition to Pseudomonas aeruginosa, Nocardia asteroids, and Candida albicans strains have been more effective for ethyl acetate than chloroform and methanol fractions, however, lower concentrations of chloroform fractions confirmed higher sensitivity in opposition to Candida albicans.

**Antioxidant activity: -**Antioxidant activities of three morph forms of Thevetia peruviana, and Juss fruit wall extracts were evaluated using a DPPH free radical scavenging assay. Petroleum ether, chloroform, ethyl acetate, and methanol were taken as organic solvents. DPPH free radical scavenging activity exhibited 50% inhibition for ethyl acetate fraction at a concentration of 1.2mg/ml.[29]

**Antidiabetic activity:** -The in vivo antidiabetic activity of *Pita Karavira* (Thevetia peruviana) bark was performed in streptozotocin-induced diabetic rats which showed significant activity.[29]

**Piscicidal activity:** The leaf and bark of the Thevetia peruviana plant were administered for 24 h to the freshwater fish Catla Catla (Hamilton) to evaluate their piscicidal activity in the 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. A similar trend was also observed in the case of other solvents (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 extracts in both conditions. So, the biochemical analysis is taken only acetone leaf and bark extract of Thevetia peruviana plant in laboratory conditions.

**Larvicidal activity: -**Larvicidal efficacy of methanol leaf extract of pita Karaveera (Thevetia peruviana) changed into tested in opposition to the aquatic stages of Aedes aegypti. The mortality in the population of the larval stage of mosquito was observed in opposition to I, II, III, and IV instar larvae and pupae of A. aegypti after 24 hrs. of remedy with specific concentrations (500-700ppm).

**Pesticidal activity:** -The leaf of Thevetia peruviana had been extracted in aqueous and dealt with in opposition to the adults of Holotrichia Serrata (Fab.). The examined aqueous leaf extract successfully produced 50% mortality of Holotrichia Serrata (Fab.) and their toxicity became 0.1/2% after 48 hours of bioassay.[29]

**Antifertility activity:** -The antifertility potential of methanol extract of *Pita Karavira* (Thevetia peruviana) bark was evaluated. *Pita Karaveera* (T. peruviana) stem bark methanol extract administered orally to male rats causes a significant reduction inside the reproductive organs. A considerable fall in the overall protein and sialic acid content material of the testes, epididymides, seminal vesicles, and ventral prostate. The extract of *Pita Karavira* bark additionally triggered a decline in spermatogenic factors (preleptotene and pachytene spermatocytes, secondary spermatocytes, round spermatids, and mature Leydig cells). At the stated dose level Leydig cell nuclear diameter, seminiferous tubular diameter, and Sertoli cellular region have been considerably reduced.[30]

**Antitumor activity: -** Methanol extracts of pita Karavira (Thevetia peruviana) fruit confirmed antitumor activity in opposition to Ehrlich's ascites carcinoma (EAC) cellular line in Swiss albino mice.

**Table: -** Some of the most important pharmacological properties of Thevetia peruviana plant parts in different extracts.[31]

**Table 16**

| Medicinal properties | Plant part | Extract |
|---|---|---|
| Antidiabetic | Bark | Methanol |
| Antifertility | Bark | Methanol |
| Antioxidant | Fruit | Petroleum ether, chloroform, ethyl acetate, and methanol |
| Anticancer | Fruit | Methanol |
| Larvicidal | Leaves | Petroleum ether, chloroform, acetone, and methanol |
| Antimicrobial | Seed | chloroform, ethyl acetate, and methanol |

**Phytochemistry:** - *Thevetia peruviana* seed kernels are very rich in cardioactive glycosides, trioxides i.e., the aglycone of those glycosides includes 3 sugar units. The most essential constitutional glycoside is thevetin. Thevetin is a mixture of trioxides specifically Thevetin A and Thevetin B (Cerebroside). Seed kernels moreover consist of neriifolin, acetyl neriifolin, thevofoline, theveneriin, and peruvoside which may be monoxide in nature. Fatty oils represent more than 62% of the seed kernel. Seed additionally includes a small quantity of theveside, viridoside, and perusitin. Apigenin-5-methyl ether has been isolated from seed shells. A number of flavonol glycosides of kaempferol and quercetin have been isolated from the leaves. Leaves also incorporate polyhydroxy-Dino monoterpenoids and their apiosylglucosides. Epiperuviol acetate, hesperidin-7-glucoside, α-and β-amyrin, kaempferol, and quercetin have been isolated from fruit pericarp and vegetation.

**Mode of action (*Karmukatva*)**

Nerin, Oleandrin, and Odorin are glycosides that have digitalis-like action.

Fatal Dose- 8 to 10 seeds, 15 to 20 gm of the root, and 5 to 10 leaves.

Fatal period- 20 to 36 hrs.

**Medicinal uses:** - Different parts of Thevetia peruviana are acknowledged to possess numerous medicinal properties. The plant is typically utilized in home remedies in tropical the United States and tropical Asia. Thevetia peruviana is used traditionally in the treatment of amenorrhoea, malarial fever, jaundice, hemorrhoids, constipation, headaches, skin issues, and so forth. The primary medically active compounds observed in the plant are various cardiac glycosides, of these glycosides, peruvoside has been investigated thoroughly. Large-scale scientific trials confirmed that each form of cardiac insufficiency can be successfully treated with peruvoside of the alternative glycosides, thevetin has successfully been used clinically in cases of cardiac decompensation, even though its effective dose is an alternative

close to its poisonous dose. Thevetin A is far less potent than combination thevetin. The efficiency of neriifolin as a cardiac glycoside is only mild. Latex is carried out to decayed teeth to relieve toothache and is used to deal with chronic sores and ulcers. The bark is an effective antiperiodic and febrifuge. A tincture of the bark is used in the remedy of malarial fever and snakebites. Water, wherein the leaves and bark had been macerated, is taken to remedy amenorrhoea. A decoction of the leaves is taken to deal with jaundice and fever and as a purgative for intestinal worms. The leaf sap is used as eye drops and nose drops to remedy violent headaches. The seeds can be used as a purgative at the same time as treating rheumatism and dropsy and as an abortifacient. The pulverized seeds are from time to time an ingredient in suppositories to alleviate hemorrhoids. The oil from the kernel is applied topically to deal with skin complaints.

**Table 17: Traditional uses of different parts of thevetia peruviana.**

| Plant parts | Traditional uses |
|---|---|
| Stem bark | Malarial fever, snake bites, febrifuge, purgative, emetic, intermittent fever, sores, amenorrhoea |
| Seeds | Abortifacient, emetic, haemorrhoids, skin complaints, used as a purgative when treating rheumatism and dropsy |
| Leaves | Jaundice, fever, as a purgative for intestinal worms, as eye drops and nose, drops to cure violent headaches, colds |
| Roots | Snakebites, made into a plaster and applied to the tumor. |
| Fruits | Used in ointments and liniments |

**Post mortem appearance**

Non-specific-findings. Petechial hemorrhages at the coronary heart are a characteristic feature. Organa is congested. In the case of yellow oleander- signs and symptoms of GIT irritation may be visible. The stomach and duodenum may be congested and might show fragments of seeds. Congestion of visceral organs is visible.[32]

**Medico-legal importance**

Suicide is common amongst village women, the use of it as a paste or decoction.[33]

1. It is used as an abortifacient, applied both locally and internally.
2. Homicide is rare.
3. Accidental poisoning is occasionally met with when decoction is used:
4. Externally to reduce swelling.
5. As a remedy for venereal diseases.
6. As a love-philter (Increases attraction among the giver and taker**.**

## CONCLUSION

Karaveera, known as an Upaviṣa in Ayurvedic medicine, is used for various diseases, particularly Kuṣṭha (Leprosy). Different parts of the plant, including Pita Karaveera (Thevetia peruviana), possess pharmacological properties that lack sufficient scientific research. Classical texts on Karaveera have not been comprehensively reviewed, highlighting the need for systematic investigation. The plant contains active compounds like cardiac glycosides, particularly peruvoside, which have been well-studied. Its bark tincture is used for malarial fever and snakebites, while macerated leaves and bark treat amenorrhea. A decoction of leaves helps with jaundice, fever, and intestinal worms. More research is essential to explore its medicinal value for mankind. Suicide is common amongst village women, the use of it as a paste or decoction. So, it is also important in Medico-legal cases.

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