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Review Article

Scientific Update on the Pharmacognostic, Pharmacological and Phytochemical Properties of *Thevetia peruviana*

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ABSTRACT

The human race has embraced technology to a great extent in the modern world of living things. Although advanced technologies are great, they also produce a great deal of disease in the human health care system, where India has achieved ranking of 4th, 5th, and even 2nd in the globe. The purpose of this review is to condense the existing scientific and molecular information about *Thevetia peruviana*, including its pharmacognostic characteristics, pharmacological potential, phytochemical qualities, and potential future research areas. Using Google, PubMed, Scholar, and other web resources, data were gathered.

Keywords: *Thevetia peruviana*, Pharmacognosy, Pharmacology, India, Future scope.

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INTRODUCTION

The term "medicinal plant" refers to many different plant species utilised in herbalism ("herbology" or "herbal medicine"). It involves both the study of and use of plants for therapeutic purposes.[1] The Latin word "herba" and the old French word "herbe" are the origins of the word "herb." Today, the term "herb" is used to describe any component of the plant, including the fruit, seed, stem, bark, flower, leaf, stigma, or root of a non-woody plant. Before, only non-woody plants, such as those that come from trees and bushes, were referred to as "herbs." these healing plants are also utilised in some types of spiritual practices, as well as in food, flavonoids, medication, and perfume.[2]

The World Health Organization estimates that roughly 80% of the 5.2 billion people in the world reside in less developed nations and that among them, traditional medicine accounts for practically all of their basic healthcare requirements. More than 3.3 billion people in the less developed countries regularly use medicinal plants since they represent the "backbone" of traditional medicine.[3] Nearly all of the world's 2,000 ethnic groups have their own unique traditional medical knowledge and experiences.[4,5] The tropical forests are home to roughly half (125 000) of the world's blooming plant species. There is still a huge pool of potential medicine species in tropical rain forests. They continue to give natural product chemists priceless molecules to use as building blocks when creating novel medications. Due to the fact that just 1% of tropical species have been investigated for their potential as pharmaceuticals, there is a tremendous possibility for discovering additional chemicals.[6]

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According to the literature review, it is concluded that there is a dearth of comprehensive scientific information on *Thevetia peruviana* (*T. peruviana*) and that the compiled data may be used as a supporting resource for future research on the plant's anatomy and physiology, the development of formulations, the preparation of monographs, and as a foundation for the future treatment of many diseases.

Apocynaceae is the family of small ornamental shrubs that includes *T. peruviana*. Because of its yellow blossoms, it is also known as Pillikaner or Yellow Oleander and can be found all over India.[7] It is also known as milk bush, yellow oleander, fortunate nut, and kaner. It is an evergreen shrub that is common in subtropical and tropical forests around the world.[8] There are two types of the plant: *Nerium oleander*, which has purple blooms, and yellow oleander, which has yellow flowers. Throughout the entire year, both types of flowers and fruits offer a consistent supply of seeds. When planted in hedges, they can produce 400–800 fruits annually, depending on the type of rainfall and plant age. The spherical fruits are typically green in hue but turn black as they ripen. Each fruit includes a nut and can have one to four seeds in its kernel when dissected longitudinally and transversely. These plants produce milky liquid in all of the organs, and they get hazardous due to the presence of cardiac glycosides such nerifolin and peruvoside.[9] The fruit contains a milky fluid that contains thevetin, a chemical used to stimulate the heart. In their natural state, all plant parts are exceedingly dangerous, but seeds in particular. A huge flowering shrub called *T. peruviana* can handle most types of soil and is drought resistant. If desired, it can be grown outside as a shrub or tree in warmer climates. these plants can handle most soil types as long as they are well-drained and kept in full sunlight in a protected area. It is helpful in warmer climates because it may be used as a landscaping plant and doesn't need much upkeep.[10]

Plant Profiling

Taxonomy Classification[11]

Kingdom : Plantae

Subkingdom : Tracheobionta

Super division : Spermatophyta

Division : Magnoliophyta

Class : Magnoliopsida

Subclass : Asteridae

Order : Gentianales

Family : Apocynaceae

Genus : *Thevetia*

Species : *peruviana*[Figure 1]

Vernacular names[11]

Hindi: PeeliKaner, kulkephul

Tamil: Thiruvachipoo, Ponnarali

Bengal: Kolkaphul

Marathi: Bitti

Manipuri: Utonglei

Others: Manjaaralie, Shatakunda, Pachaganeru, Ponnarali, Ashvaghna, Ashvamaraka

Figure 1: Thevetia peruviana.

Synonyms

Cascabelathevetia, Cerberathevetia, Thevetia neriifolia.[11]

Common name

Be-still tree, suicide tree, lucky nut.[11]

Habitat: Tropical, lowland areas.[11]

Agriculture

T. peruviana is grown for ornamental purposes, and in temperate climates, it is typically planted as a large flowering shrub or small ornamental tree standard in gardens and parks. For many years, missionaries and explorers have grown as a decorative plant in temples, residences, schools, gardens, churches, and by the sides of roads. Though widely cultivated in tropical and subtropical areas of the world, it is most likely native to central and South America.[12]

Traditional uses

Traditionally *T. peruviana* bark used in case of malarial fever, snake bites, febrifuge, purgative, emetic, intermittent fever, sores, amenorrhea. Seeds are used as abortifacient, emetic, hemorrhoids, skin complaints, used as a purgative when treating rheumatism and leaves are used as a jaundice, fever, as a purgative for intestinal worms, as eye drops and nose drops to cure violent headaches, colds.

Pharmacognostic standardization of *T. peruviana*

The pharmacognostic features of *T. peruviana* are shown in Table 1 in which complete observation of flower, leaf and fruit are given.[13] Table 2 shows the various chemical constituent and their retention index present in volatile oil of *T. peruviana* (Figures 2A, 2B and 2C).[13]

Figure 2: *T. peruviana* fruits, Figure 2B: *T. peruviana* flower, Figure 2C: *T. peruviana* leaves.

Table 1: Morphology of flower, leave and fruit.

Sl.no.	Parameter	Flower observation	Leave Observation	Fruit Observation
1.	Shape and Structure	Narrow funnel shaped with swird petals	Spirally arranged	Globular
2.	Odour	Pleasant Smell	Sweet Scent	Unpleasant
3.	Color	Yellowish, Yellowish green, Dark Yellow	glossy green	Green Color
4.	Touch	Smooth	Smooth	Smooth
5.	Size	6.7×2.3 cm	13-15 cm in length	4 cm
6.	Taste	Sweetish, Pleasant	Bitter	Highly poisonous

Table 2: Chemical constituent present in *T. peruviana*.

Compounds	KI	Percentage
Camphor	1054	7.42
Camphene	967	0.09
Ocimene	1063	0.92
Cis-carvioldihydro	1103	8.98
Hexyl butanoate	1294	0.73
Linalool	1322	23.07
D-glucitol	1487	1.09
Farnesene	1587	0.73
Caryophyllene oxide	1535	0.21
Linalyl acetate	1327	3.04

Pharmacological Investigate and molecular analysis

Anti-diarrheal

Hassan and others studied the anti-diarrheal properties of ethanol-extracted yellow oleander leaves (*T. peruviana*). In a model of albino rats, the extract was evaluated against castor oil-induced diarrhea and demonstrated considerable anti-diarrheal action (*p*-0.01). Before the experiment began, the rats were acclimated for one week to conventional laboratory settings (temperature 241°C, relative humidity 555%, and a 12-hr photoperiod) in suspended wire-meshed galvanised cages (4-6 rats/cage).[14]

Anti-bacterial activity

Hassan and others concentrated on the extract's antibacterial properties, which were ineffective against both Gram positive and Gram-negative microorganisms (mainly Bacillus sp). yellow oleander leaves extracted with ethanol demonstrated a restricted zone of inhibition against *Shigellaflexineri, Salmonella typhi, klebsiella* sp., *Staphylococcus aureus,* and *Shigellasonnei* bacterial lawns. The plant extract's cytotoxicty was tested on brine shrimp nauplii, and the LC_{50} value was found to be 627.21 g/ml. the extract's safety effect is indicated by the wide range of the LC_{50} value.[14] Anupama *et al*. also investigated *T. peruviana* crude extracts with varying levels of antioxidant and antibacterial activity. The antioxidant and antibacterial activity of several plant sections was tested using aqueous and alcoholic crude extracts, and it was discovered that methanol extracts of *T. peruviana* showed a substantial antioxidant activity.[15,35,36] By using an agar well diffusion test, Alisha and her team determined the antimicrobial potential of *T. peruviana* latex against *Bacillus subtilis*, *Staphylococcus aurens*, *Pseudomonas anuginosa*, and *E. coli*, as well as filamentous black fungus (Mucorcircinelloids),and unicellular fungus (*Candida albicans*).[18,22,36,37]

Cytotoxic activity

Hassan and others were determined the cytotoxic activity of yellow oleander leaf extract by using a brine shrimp lethality experiment. A dose-dependent lethality was observed in the percentage mortality of brine shrimp at six different doses of the extract of yellow oleander leaves. More specifically, mortality rates of 0, 5, 10, 35, 65, and 100% were seen at 62.5, 125, 250, 500, 1000, and 2000 g/ml.[14]

Anti-cancer activity

Alberto Ramos-Silva and team used the MTT assay to evaluate the *T. peruviana* fruit methanolic extract's anticancer potential. On all tested cancer cell lines, the extract significantly reduced cell motility and colony formation.[16]

Using the MTT method, Aisha and team examined the anticancer potential of *T. peruviana* latex against the prostate cancer cell (PC3) and breast cancer cell (MCF7). They discovered that PT was 97.11% toxic to PC3 and 96.11% toxic to MCF7, with 1000 g/ml iota IC_{50} values of 48.26 g/ml and 40.31 g/ml, respectively. Recent studies have shown unequivocally that latex has many components that are highly effective in fighting cancer.[18,25-28]

Chemical Profiling

Salma A. and team investigated the chemical profiling of *T. peruviana* leaves by micro invulsion formulation and concluded that it's a safe cytotoxic agent and active against HEPG2 and MCF7 cell lines. The LD_{50} to be 3.083 g/kg and IC_{50} was 25 to 65 µg/ml and 3.58 µg/ml for MCF7 and HEPG2 cell line respectively.[17]

Anti-coagulant activity

Prothrombin time and activated partial thromboplastine time tests were used by Aisha and team to examine the *invitro* anti-coagulant activity of PT latex, and they came to the conclusion that the PT latex had good anti-coagulant activity.[18,29-32]

Anti-fungal activity

T. peruviana seed samples were examined for their photo activity as an antifungal. Column chromatography was used to fractionate extracts made from either n-hexane or dichloromethane, which were then subjected to thin-layer chromatography for additional analysis. *Cladosporium cucumerinum* was evaluated for inhibition by all seed extracts and fractions in order to assess their photoactive inhibitory activities. To determine its components, capillary gas chromatography with mass spectrometry was used to analyse the most photoactive fraction.[19]

Juvenomimetic activity

Bai H. and team was investigated the Fresh *T. neriifolia* leaves and seeds were investigated for their ability to function as juvenomimetic agents against the red cotton insect, dsydercus cingulatus, a significant pest of cotton and okra. 40% leaf and 10% seed extracts showed noticeable activity based on larval mortality, length of the ovipositional phase, the appearance of deformed adults, and reduced fecundity of the bugs. Although 20% leaf and 5% seed extracts showed some action, 10% leaf and 2.5% seed extract treatments had no discernible impact.[20]

Anti-hemolysis activity

Erythrocyte membrane stabilisation, a method for evaluating a substance's capacity to reduce inflammation, was studied by Aisha and team. This method was used in the current research was conducted under hypotonic conditions, which led to cell lysis. As latex concentrations increased, hemolysis inhibition percentage increased as well, but it didn't reach 58.5% until the highest concentration of 1000 g/ml. Hemolysis inhibition could result from the presence of one or more natural compounds in latex. The greatest hemolysis inhibition was found to be obtained at 91.0% when indomethacin was utilised as a positive control for latex's effectiveness at 200 g/ml. The latexes of *T. peruviana* and calotropisprocera have been shown to have anti-inflammatory effec.[21,33]

Molecular docking study

Aisha and colleagues concentrated on a molecular docking research of, routine against the 3QUM and 1JNX receptor for cancer and discovered that the values of the docking scores against the 3QUM and 1JNX were, respectively, -6.87 and -6.97 kcal.mol-1.[18,22,23,24]

Gastro Protective activity

With ethanol-induced and indomethacin-induced gastric lesions as their models, Pragati and team concentrated on the gastro protective effects of *T. peruviana* and came to the conclusion that it has such activity.[39]

Locomotor activity

Pragati and her team looked into the *T. peruviana's* locomotor behavior. *In comparison to mice* treated with vehicle (2012 ± 497 counts in 90 min), locomotor activity was seen in mice after treatment oil was either provided orally at a dose of 100 mg/kg (2347 ± 567 counts in 90 min) or inhaled for 60 min (2767 ± 756 counts in 90 min).[39]

Piscicidal activity

On Catla Catla (Hamilton), *T. peruviana* leaf and bark were applied for 24 hr. To assess the piscicidal activity, two conditions were used: a. laboratory condition and b. a cemented pond condition. Different solvents, such as acetone, diethyl ether, ethyl alcohol, chloroform, and carbon tetrachloride, are utilised in both circumstances. Acetone leaf extract and acetone bark extract of *T. peruviana* have distinct LC_{50} values. Acetone leaf extract has a value of 88.80 mg/L (24 hr) in a laboratory setting and 529.38 mg/L (24 hr) in a cemented pond. Acetone bark has a value of 9943 mg/L (24 hr) in a laboratory setting and 591.78 mg/L (24 hr) in a cemented pond when compared to freshwater fish catla catla. Similar to that, the entire procedure was witnessed using several solvent kinds, however the acetone bark and leaf extract is far more efficient than other solvents.[40-43,45]

Anti-spermatogenic activity

Koushik and team investigated the *T. peruviana* antifertility ability demonstrates that the male albino rat spermatogenesis is inhibited. Thevetigenin, lupeol, -amyrin, -amyrin, and lupeol are the active ingredients that are in charge of the anti-spermatogenic activity. Orally administered 100 mg/rat/day of *T. peruviana* stem bark methanol extract (TPMTE) to male albino rats. In reproductive organs (such as the testes, epididymides, seminal vesicle, and ventral prostate), protein and sialic acid levels are lowered, and cholesterol levels are elevated. Reduces the sertoli area, seminiferous tubular diameter, and nuclear diameter of leydig cells (*p* 0.001). According to the results of the study, *T. peruviana* is a natural contraceptive that also inhibits spermatogenesis in rats.[40-42,44,45]

Anti-diabetic activity

Tabrez and *et al.* focused on the *T. peruviana* bark was tested for *in vivo* anti-diabetic action in streptozotocin-induced diabetic rats, and it demonstrated considerable effectiveness in a concentration-dependent manner.[46]

Larvicidal activity

T. peruviana leaf extract in methanol was put to the test against the larval stages of *A. aegypti*. After 24 hr of treatment with various concentrations, the mortality of *A. aegypti* I, II, III, and IV instar larvae and pupae was observed (500-700ppm). The *A. aegypti* larvae in this study's IV instar showed less vulnerability than pupae and larval stages. Concentrations led to a rise in mortality, and the larvae also slowly develop malanization.[47]

T. peruviana leaf extracts were utilised to research the plant's larvicidal abilities against the larvae of the dengue (*Aedes aegypti*) and malaria (*Anopheles stephensi*) vectors. After 24 hr, the mean LC_{50} values for the petroleum ether, chloroform, acetone, and methanol extracts of *T. peruviana* leaves against the larvae of *A. stephensi* and *A. aegypti* mosquitoes were determined to be 0.045, >0.05, 0.026, 0041 and 0.038, >0.05, 0.021, and 0.036%, respectively. Chloroform extract's delayed effect after 3 days showed that the larvicidal action is likely caused by the prevention of insect development.[48]

Anti-tumor activity

Tabrez and *et al*. focused on Swiss albino mice treated with methanol extracts of *T. peruviana* fruit exhibited anticancer efficacy against the Ehrlich's ascites carcinoma (EAC) cell line. Comparatively to the EAC control group, the extract-treated group's tumor volume, tumor weight, and viable cell count were reduced. For the extract-treated groups (50mg/kg and 100mg/kg body weight), the tumor volumes were 3.62 0.12 ml, 2.88 0.23 ml, and 1.34 0.17 ml, respectively. In comparison to the EAC control group, the extract dramatically (P 0.001) reduced lipid peroxidation and restored reduced glutathione, superoxide dismutase, and catalase to normal levels.[49]

An investigation into TRAIL resistance-busting behavior was conducted. In human gastric cancer cells, cardenolide glycosides from *T. peruviana* were found to significantly reverse TRAIL resistance, and real-time PCR results revealed that thevefolin increased mRNA expression of death receptors 4 (DR4) and 5 (DR5). Thevefolin's 1H and 13C NMR characterizations are also displayed.[50]

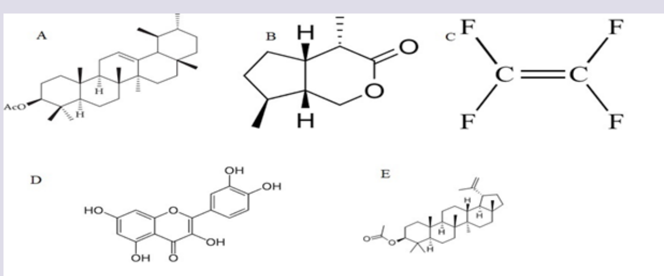

Figure 3: Chemical constituent present in *T. peruviana.*

Analytical Analysis

High-performance liquid chromatography (HPLC)

HPLC analysis was done following (Kim *et al*., 2006) utilising a liquid chromatograph from the Agilent Technologies 1100 series with a diode-array detector. C_{18} guard column and Eclipse XDB-C_{18} (150 4.6 mm, 5 mm) column were employed (Phenomenex, Torrance, CA). The acetonitrile (A) mobile phase contained 2% acetic acid in water (v/v) (B). The whole runtime was 70 min, with a flow rate of 0.8 ml/min. The gradient programme went from 100% to 85% in 30 min, from 85% to 50% in 20 min, from 50% to 0% in 5 min, and from 0% to 100% in 5 min. 50 l was the injection volume. Peaks for the derivatives of benzoic acid and cinnamic acid were observed at 280, 320, and 360 nm. Peaks were noted when UV Spectra and retention durations were compared to standards.[17]

Gas chromatography analysis

Pet. ether (MEF) significantly improved its ability to kill breast cancer cells, with an IC_{50} (g/ml) reduction from 25 to 6.5 and all the benefits of microparticle size. On the other hand, little research has been done to date to examine the chemical makeup of this species' lipoidal matter. As a result, we attempt to provide a thorough understanding of its chemical makeup by saponifying pet. Ether extract into unsaponifiable fraction and saponifiable fraction.[17]

Structure and chemical constituent of T. peruviana

Iridoidglucosides, thevetile, and derivatives of quercetin, as well as pervoanosides I–III, and kaempferol: thevefolin, theviridoside derivatives from plant leaves, and perivianusenyl acetate A-C, lupidienyl acetate, amyrin acetate, and lupeol acetate are examples of ursane type triterpenes. (Figures 3A, 3B, 3C, 3D and 3E).[50]

Future prospects

There are a number of primary and secondary metabolites in the plant *T. peruviana* that are responsible for treating a number of acute and chronic disorders; thus, there are a number of pharmacological activities that have not yet been described. The fresh researchers may find it simple to understand those activities for the best plant investigation. Numerous phytochemicals have been found in different areas of *T. peruviana*; they may be able to treat ailments and provide new research opportunities in the future.

CONCLUSION

The human population currently relies on herbal remedies to treat illnesses, and they choose herbal medications for their main effects simply because they have less side effects. Despite having a lot of pharmacological activity and being a lovely ornamental plant, *T. peruviana* has been determined to be safe at various levels of investigation. The plant's pharmacognostic parameters demonstrated its anatomy and physiology, and HPLC and Gas chromatography testing demonstrated that *T. peruviana* is a good source of the Vitamins B_6 potassium, and calcium needed to treat a variety of ailments, including obesity, gastrointestinal disorders, and inflammatory diseases. The plant has important characteristics that serve as the foundation of numerous research fields, thus it requires careful social research.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

ABBREVIATIONS

T. peruviana: *Thevetia peruviana*; ***A. aegypti:*** *Aedes aegypti*; ***T. nerriifolia:*** *Thevetia neriifolia*; ***A. stephensi:*** *Anopheles stephensi*; **HPLC:** High-performance liquid chromatography; **GCMS:** Gas chromatography.

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