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## A REVIEW ON PHYTOCHEMICAL, PHARMACOLOGICAL STUDY ON POISONOUS PLANT OF *THEVETIA PERUVINA*.

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### ABSTRACT

*Thevetia peruviana*, widely recognized as the Lucky Nut, is a highly toxic plant with significant pharmacological potential, belonging to the Apocynaceae family. This plant is a reservoir of diverse bioactive compounds, notably cardiac glycosides such as thevetin A and thevetin B, which possess therapeutic properties but are associated with high toxicity. Its phytochemical composition also includes alkaloids, flavonoids, saponins, and tannins, which contribute to its antimicrobial, anti-inflammatory, antioxidant, and anticancer effects. However, the plant's pharmacological utility is constrained by limited knowledge of its pharmacokinetics—encompassing absorption, distribution, metabolism, and excretion (ADME)—and a lack of detailed understanding of the molecular mechanisms behind its actions. This study delves into the phytochemical makeup, pharmacokinetic profile, pharmacological activities, and molecular interactions of *Thevetia peruviana*. It identifies critical research gaps and underscores the necessity for advanced investigations to mitigate its toxicity while maximizing its therapeutic potential, thus addressing its dualistic nature.

**Keywords:** *Thevetia peruviana*, pharmacokinetic, phytochemical, Apocynaceae etc.

### INTRODUCTION

*Thevetia peruviana*, commonly known as the Lucky Nut, is a widely distributed ornamental plant belonging to the

Apocynaceae family. Native to Central and South America, this plant has gained significant attention due to its dual nature as

a source of therapeutic potential and a toxic agent. Despite its aesthetic appeal and traditional use in medicine, *Thevetia peruviana* is considered a poisonous plant because of the presence of potent cardiac glycosides. These glycosides, primarily thevetin A and thevetin B, have been identified as the principal bioactive compounds responsible for both its pharmacological properties and toxic effects. The plant has a long history of being used in traditional medicine to treat conditions such as skin infections, inflammation, and heart ailments. However, its toxic potential poses a significant challenge to its safe and effective application [1].

Phytochemical investigations of *Thevetia peruviana* have revealed a diverse array of secondary metabolites, including alkaloids, flavonoids, saponins, tannins, and cardiac glycosides. These bioactive compounds are responsible for the plant's pharmacological activities, such as antimicrobial, anti-inflammatory, antioxidant, and anticancer properties. Nonetheless, the therapeutic potential of *Thevetia peruviana* remains underutilized, largely due to its toxicity and the lack of comprehensive pharmacokinetic and molecular studies to elucidate its mechanisms of action and metabolic

pathways. Understanding the phytochemical composition and pharmacokinetic behaviour of these compounds is crucial for developing safe and effective therapeutic applications of this plant [2].

From a pharmacokinetic perspective, the absorption, distribution, metabolism, and excretion (ADME) of *Thevetia peruviana*'s bioactive compounds have not been fully explored. Investigating these parameters is essential for determining their bioavailability, therapeutic efficacy, and potential adverse effects. Similarly, molecular studies can provide insights into the interactions of these compounds with biological targets, paving the way for the development of novel drug candidates. Such studies could also help in mitigating the toxic effects of the plant by identifying safer dosage forms or developing derivatives with reduced toxicity [3].

This review aims to provide a comprehensive analysis of the phytochemical, pharmacokinetic, pharmacological, and molecular aspects of *Thevetia peruviana*. By integrating existing knowledge and highlighting research gaps, this study seeks to foster a deeper understanding of the plant's dualistic nature, enabling its safe and effective utilization in pharmacological applications while addressing its toxicological concerns [4].

**MORPHOLOGY OF *THEVETIA PERUVIANA* (Figure 1)**

Figure 1: Morphology of *Thevetia peruviana*

**Height:** *Thevetia peruviana* is typically grows to a height of 2-5 meters (6.5-16.5 feet), making it a medium-sized ornamental shrub or small tree.

- **Leaves:** *Thevetia peruviana* leaves are long, narrow, lanceolate, and glossy green, measuring 8-15 cm in length. They are arranged alternately and contribute to the plant's lush, ornamental appearance [5].
- **Flowers:** *Thevetia peruviana* flowers are trumpet-shaped, fragrant, and typically yellow or peach in color. Blooming throughout the year, they attract pollinators and add ornamental beauty to gardens and landscapes.
- **Fruits:** *Thevetia peruviana* fruits are green when unripe, turning black upon maturation. They are drupes with a hard, woody seed inside. The fruit is toxic due to cardiac glycosides, making it harmful if ingested by humans or animals.
- **Stem:** *Thevetia peruviana* stems are slender, green when young, and turn woody and brown with age. They exude a milky sap when cut, which contains toxic compounds. The stems support the plant's bushy, ornamental structure and dense foliage.
- **Seeds:** *Thevetia peruviana* seeds are hard, woody, and enclosed within the fruit's tough outer shell. Typically dark brown, they contain toxic cardiac glycosides. Despite their toxicity, the seeds are sometimes used in traditional crafts and jewelry for their unique appearance.
- **Habitat:** *Thevetia peruviana* thrives in tropical and subtropical regions, often found in gardens, roadsides, and open spaces. It prefers well-drained soils and tolerates a range of conditions, from sandy to loamy substrates. The plant is drought-resistant and grows well in full sunlight, making it suitable for arid and

semi-arid environments. Native to Central and South America, it has become naturalized in many parts of Asia, Africa, and Australia.

- **Cultivation:** *Thevetia peruviana*, or yellow oleander, is cultivated primarily for its attractive appearance and hardiness. It thrives in tropical and subtropical regions, preferring well-drained, fertile soils, though it can tolerate sandy or loamy conditions. Full sunlight is ideal for optimal growth, but it can also survive in partial shade. The plant is drought-tolerant once established, requiring minimal irrigation once mature. Propagation is typically done from seeds or cuttings. Seeds are sown in warm, moist soil, and they germinate relatively quickly, while cuttings root easily in a sandy, well-drained medium. Regular pruning encourages compact, bushy growth and helps maintain its shape. Fertilizing during the growing season can enhance flowering and overall vigor. Despite being low-maintenance, *Thevetia peruviana* must be handled with care due to its toxicity, particularly the seeds and sap. This makes it unsuitable for areas accessible to children or pets. It is a popular choice for ornamental plantings, hedges, and roadside beautification [6, 7].

- **Chemical Constituents:** *Thevetia peruviana* contains several bioactive chemical constituents, particularly cardiac glycosides, which are responsible for its toxicity. The most notable glycosides in the plant include thevetin A, thevetin B, and peruvoside. These compounds have potent cardiotoxic effects, interfering with the heart's electrical activity and potentially causing arrhythmias, making the plant hazardous to humans and animals if ingested. In addition to cardiac glycosides, *Thevetia peruviana* contains alkaloids, flavonoids, saponins, and phenolic compounds. The sap of the plant contains toxic resinous substances that can cause skin irritation. The leaves and seeds also contain high concentrations of these toxic compounds, especially in their unripe stages. While the plant is mainly considered toxic, some of its constituents have been studied for their potential therapeutic effects, including anti-inflammatory and anti-cancer properties. However, due to the risks associated with its toxicity, *Thevetia peruviana* is primarily utilized for ornamental purposes rather than medicinal use [8].
- **Leaves:** The leaves of *Thevetia peruviana* contain several potent

chemical constituents, primarily cardiac glycosides, which are responsible for the plant's toxicity. Key glycosides in the leaves include thevetin A and thevetin B, both of which affect the heart by inhibiting the sodium-potassium ATPase pump, leading to potential cardiac arrhythmias and other heart disturbances if ingested. These compounds are found in high concentrations in the leaves, making them particularly dangerous. Additionally, *Thevetia peruviana* leaves contain alkaloids, which contribute to their toxic properties. Flavonoids and phenolic compounds are also present, known for their antioxidant and anti-inflammatory effects, although their concentrations are much lower than the glycosides. Saponins, which are mildly toxic, have been identified in the leaves as well, and they can cause irritation if they come into contact with the skin. Due to these toxic constituents, *Thevetia peruviana* should be handled with caution, especially when cultivating or using parts of the plant for ornamental purposes.

- **Bark:** The bark of *Thevetia peruviana* contains several toxic chemical constituents, with the most significant being cardiac glycosides, including

thevetin A and thevetin B. These glycosides are responsible for the plant's cardiotoxicity, as they interfere with the sodium-potassium pump in heart cells, potentially leading to arrhythmias or other heart-related complications if ingested or improperly handled. The concentration of these compounds in the bark is lower compared to the leaves or seeds, but they still pose a significant health risk. In addition to cardiac glycosides, the bark also contains alkaloids, which contribute to its toxic properties. The sap from the bark may contain resinous compounds that are irritating to the skin and mucous membranes. Phenolic compounds and flavonoids, which possess antioxidant properties, are also found in small amounts in the bark. Due to these harmful constituents, the bark of *Thevetia peruviana* should be handled with care and avoided for consumption or unprotected skin contact [9].

- **Fruit Pericarp and Flowers:** The fruit pericarp (outer layer) and flowers of *Thevetia peruviana* contain several bioactive chemical constituents, though they are less concentrated than in the seeds or leaves. The fruit pericarp contains cardiac glycosides, including thevetin A and thevetin B, which are

toxic and can lead to serious cardiac disturbances if ingested. These compounds are present in smaller quantities compared to other plant parts, but caution is still necessary. The flowers of *Thevetia peruviana* are primarily known for their attractive appearance and fragrance but also contain toxic compounds, including low concentrations of alkaloids, flavonoids, and saponins. These components can contribute to mild toxicity if consumed in large quantities, though they are not as potent as those found in the seeds or leaves. Additionally, the flowers have some antioxidant properties due to the presence of phenolic compounds. Despite these constituents, the fruit pericarp and flowers are not commonly used for medicinal purposes due to the plant's toxicity [10].

- **Seed:** The seeds of *Thevetia peruviana* are particularly rich in toxic chemical constituents, most notably cardiac glycosides, including thevetin A,

thevetin B, and peruvoside. These glycosides are the primary cause of the plant's toxicity. They inhibit the sodium-potassium ATPase enzyme in the heart muscle, leading to potentially fatal arrhythmias, cardiac arrest, and other heart-related complications if ingested. The concentration of these glycosides in the seeds is high, making them especially dangerous. In addition to cardiac glycosides, *Thevetia peruviana* seeds contain alkaloids, which may contribute to the plant's overall toxicity. Saponins, which can cause gastrointestinal irritation and toxicity if consumed, are also present. Phenolic compounds with antioxidant properties are found in lower concentrations. The seeds are hard and surrounded by a toxic, resinous coating that can cause skin irritation upon contact. Due to the significant health risks associated with the seeds, they are not used medicinally and should be handled with extreme care [11].

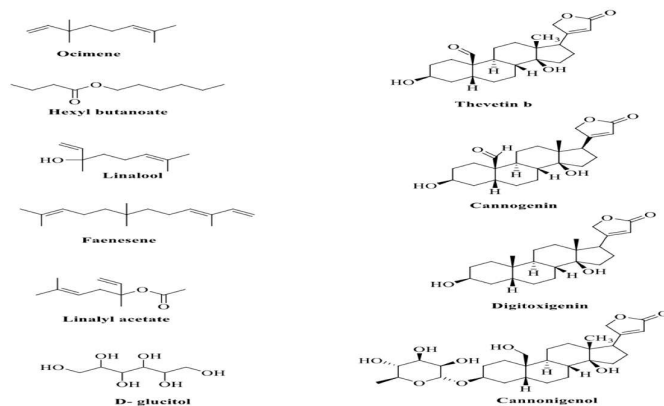


Figure 2: Some chemical constituents of *Thevetia peruviana*

**Toxicology:** *Thevetia peruviana*, commonly known as yellow oleander, is highly toxic due to the presence of cardiac glycosides, primarily thevetin A, thevetin B, and peruvoside, found in all parts of the plant, but particularly in the seeds, leaves, and bark. These glycosides interfere with the sodium-potassium ATPase pump, disrupting the normal electrical conduction of the heart and leading to dangerous arrhythmias, bradycardia, and even cardiac arrest. This makes ingestion of any part of the plant, particularly the seeds, a serious health risk. Symptoms of poisoning can appear within hours of ingestion and typically include nausea, vomiting, abdominal pain, diarrhea, and confusion. As the toxins affect the heart, patients may experience irregular heartbeats, low blood pressure, and in severe cases, cardiac collapse. Toxicity may also cause visual disturbances, dizziness, and weakness. Ingestion of even small amounts can be fatal, especially in children or animals [12]. Despite its toxicity, certain compounds in *Thevetia peruviana* have been studied for their potential medicinal uses, such as anti-inflammatory and anticancer properties. However, due to the high risks associated with poisoning, the plant is not recommended for direct medicinal use. Care must be taken to avoid accidental ingestion or exposure, particularly in environments

where children or animals may come into contact with it [13].

**Traditional uses:**

*Thevetia peruviana*, or yellow oleander, is primarily known for its toxicity, but in some traditional medicine systems, it has been used cautiously for various therapeutic purposes. However, due to the plant's high toxicity, its medicinal applications are limited and require careful handling. Traditionally, *Thevetia peruviana* has been employed in herbal remedies in certain cultures, particularly in parts of Central and South America, Asia, and Africa, although its use is not widespread. In traditional medicine, various parts of the plant, including leaves, flowers, bark, and seeds, have been used for their purported medicinal properties.

The seeds, although highly toxic, have been traditionally used in certain remedies, often as a last resort when other treatments have failed. They have been used in folk medicine as a purgative, diuretic, or for treating various ailments like rheumatism, but these uses are rare and considered dangerous. In some African traditional medicine, *Thevetia peruviana* has been used for its reputed anti-inflammatory and anticancer properties, though scientific validation for these uses is minimal. In some regions, its sap has been applied to wounds, though it can cause severe skin irritation. While *Thevetia peruviana* is sometimes used in traditional

remedies, the significant risk of toxicity severely limits its use. Today, its applications are largely relegated to

ornamental purposes rather than practical medicinal use, with safety as a primary concern [14, 15].

Table 1: Pharmacological uses of plant parts

Plant part	Traditional use
Leaves	<i>Thevetia peruviana</i> leaves have traditionally been used as an emetic and purgative, treating conditions like jaundice, fever, and violent headaches. They have also been used in eye and nose drops for colds. Additionally, a flavonol glycoside from the leaves has shown inhibitory effects against HIV-1 Reverse Transcriptase and HIV-1 Integrase.
Roots	Snakebites, roots are made into plaster and applied to tumours.
Seeds	The seeds of <i>Thevetia peruviana</i> are poisonous, abortifacient, and alterative. Traditionally, they have been used as an emetic, to treat hemorrhoids and skin problems, and as a laxative. They are also used as a purgative for conditions like dropsy and rheumatism.
Fruits	Ointments and liniments
Bark	Malarial fever, snake bites, purgative, emetic, sores, amenorrhoea, cathartic, febrifuge, useful in different kinds of intermittent fevers.

## PHARMACOLOGICAL ACTIVITIES

This Plant exhibits a wide range of pharmacological activities due to its rich composition of bioactive compounds, including cardiac glycosides, flavonoids, alkaloids, terpenoids, and saponins. Among its most notable pharmacological properties are its cardiotoxic effects, which are attributed to the presence of potent cardiac glycosides such as thevetin A, thevetin B, peruvoside, and neriifolin [16]. These compounds have a significant impact on the heart, influencing its contractility and rhythm, similar to digoxin. As a result, extracts of *T. peruviana* have been studied for potential applications in the treatment of heart conditions, although their narrow therapeutic index makes them highly toxic if misused.

The plant also demonstrates strong antimicrobial activity against a variety of pathogens, including bacteria and fungi. Its

extracts have shown promise in combating infections caused by *Escherichia coli*, *Staphylococcus aureus*, and *Candida* species, making it a potential source of natural antimicrobial agents [17].

Antioxidant activity is another important pharmacological property of *T. peruviana*. The plant's phenolic and flavonoid content helps neutralize free radicals, reducing oxidative stress and protecting against cellular damage [18, 19]. This antioxidant potential has implications for preventing chronic diseases, including cardiovascular diseases and certain cancers.

Furthermore, the plant exhibits antiparasitic and anthelmintic properties, making it effective against intestinal worms and parasitic infections [20]. It has also been used traditionally as a purgative and emetic, leveraging its ability to induce vomiting or clear the digestive tract. In addition, the seeds and other parts of the plant are known

for their abortifacient and uterotonic effects, although these applications must be approached with caution due to their high toxicity.

*T. peruviana* also demonstrates potential anticancer activity, with some studies suggesting that its bioactive compounds can inhibit the growth of cancer cells [21].

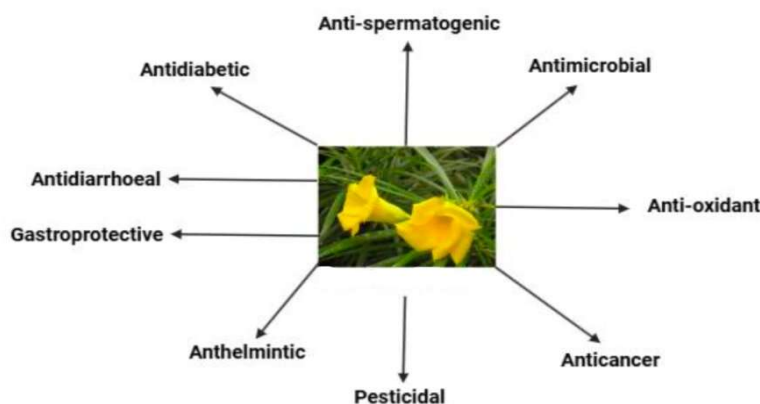


Figure 3: Pharmacological Activities of different part

### Antimicrobial activity

The plant contains various bioactive compounds, such as cardiac glycosides, flavonoids, alkaloids, and saponins, which contribute to its ability to inhibit microbial growth. Extracts from different parts of *Thevetia peruviana*, including its leaves, seeds, bark, and flowers, have been shown to exhibit antimicrobial properties against a broad spectrum of microorganisms, including bacteria, fungi, and viruses. Flavonol glycosides present in the plant, such as quercetin, have shown inhibitory effects against HIV-1 Reverse Transcriptase and HIV-1 Integrase, both crucial enzymes involved in the viral replication process. By inhibiting these enzymes, the plant's compounds may prevent the replication of the virus, offering potential as an antiviral

agent, although more clinical research is required to explore this aspect fully. The antimicrobial mechanisms of *Thevetia peruviana* are multifaceted, with its bioactive compounds causing cell membrane disruption, enzyme inhibition, and oxidative stress reduction. Despite its promising antimicrobial effects, the toxicity of *Thevetia peruviana* limits its practical use. The plant contains toxic cardiac glycosides, particularly in the seeds, which can cause serious health issues, including cardiac arrhythmias, if ingested. Therefore, while the plant has significant antimicrobial potential, its application is limited by safety concerns, and it should only be used under strict medical supervision. Further research is essential to explore the full extent of its antimicrobial properties and to find ways to

harness its benefits safely, ideally through controlled dosages or topical applications [22, 23, 24].

### Antioxidant activity

*Thevetia peruviana*, also known as yellow oleander, has been studied for its antioxidant activity due to the presence of various bioactive compounds, including flavonoids, alkaloids, and phenolic compounds. Antioxidants are substances that help neutralize free radicals, which are unstable molecules that can cause oxidative stress and damage to cells, leading to chronic diseases such as cancer, cardiovascular diseases, and neurodegenerative disorders. The plant's extracts, particularly from the leaves and seeds, have demonstrated significant antioxidant properties in laboratory studies. These findings suggest that *Thevetia peruviana* could potentially be used as a natural antioxidant in therapeutic applications to prevent oxidative damage and support overall health. However, due to the plant's toxicity, further studies are needed to determine safe and effective dosages for its antioxidant use, as excessive consumption can lead to serious health issues [25, 26].

### Antifungal Activity

The photoactive antifungal properties of *Thevetia peruviana* seedlings revealed notable effects against the fungus *Cladosporium cucumerinum*. To investigate these properties, extracts were prepared

using dichloromethane and n-hexane, and their components were further analyzed and separated using thin-layer chromatography (TLC) and column chromatography [27, 28]. These methods allowed researchers to isolate and examine the chemical decoctions, focusing on their ability to inhibit fungal growth under light-dependent conditions.

The study evaluated both the seed extracts and their fractions for antifungal activity specifically against *Cladosporium cucumerinum*. Tests demonstrated that certain crude extracts and fractions exhibited a light-dependent antifungal effect [29, 30]. This suggests that the activity of the extracts is influenced by exposure to light, making them photoactive in nature. Among the tested extracts, those produced using dichloromethane showed significant antifungal effects. Fractionation through column chromatography and further analysis with thin-layer chromatography helped isolate the active compounds responsible for this activity [31].

To better understand the photoactive inhibitory mechanisms, capillary gas chromatography coupled with mass spectrometry (GC-MS) was employed to identify the chemical constituents of the active fractions. The results highlighted the presence of a terpene compound called pulsegone as a significant component of the antifungal fraction. The findings suggest

that the observed phototoxicity against *Cladosporium cucumerinum* is at least partially attributable to the activity of pulsegone. The compound appears to play a key role in the light-dependent antifungal properties of the extracts [32].

#### **Anticancer activity**

*Thevetia peruviana*, commonly known as yellow oleander, has attracted attention for its potential anticancer properties, which are largely attributed to its bioactive compounds, including cardiac glycosides, flavonoids, and alkaloids. The antioxidant activity of *Thevetia peruviana* helps reduce oxidative stress, which is often associated with cancer development. By neutralizing free radicals, the plant's extracts may prevent the DNA damage that can lead to mutations and the initiation of cancer. Moreover, *Thevetia peruviana* has demonstrated potential in inhibiting the metastasis of cancer cells. Some studies suggest that the plant's compounds can interfere with the mechanisms that allow cancer cells to spread to other parts of the body. While these promising results indicate that *Thevetia peruviana* may have therapeutic potential in cancer treatment, its use is limited by the plant's toxicity. The cardiac glycosides in particular are highly toxic and can cause severe health issues if consumed in large amounts. Therefore, while its anticancer activity is noteworthy, further research is needed to explore the safe

and effective use of *Thevetia peruviana* in cancer therapy, potentially through targeted drug delivery systems that minimize toxicity [33, 34, 35].

#### **Antidiabetic Activity**

Research on the bark extract of *Thevetia peruviana* has shown its potential to normalize the serum biochemical profile, including reducing fat content and lowering blood glucose levels in rats, when compared to the negative control animals. Compounds from this plant family have previously demonstrated antidiabetic, hypoglycemic, and antihyperglycemic properties. The bark of *Thevetia peruviana* contains various phyto-constituents, including alkaloids, flavonoids, triterpenoids, and tannins, which may contribute to these effects [36, 37].

#### **Anti-spermatogenic Activity**

*Thevetia peruviana*, commonly known as yellow oleander, has been studied for its potential anti-spermatogenic activity, primarily due to the presence of its bioactive compounds, including cardiac glycosides, alkaloids, and flavonoids. Anti-spermatogenic activity refers to the ability of a substance to reduce or inhibit sperm production, which has led to research into its potential applications in male fertility regulation. Several studies have explored the effects of *Thevetia peruviana* on sperm count and spermatogenesis, particularly in animal models. Research suggests that the plant's compounds, particularly the cardiac

glycosides such as thevetin A and thevetin B, may affect the hypothalamic-pituitary-gonadal axis, which is responsible for regulating reproductive hormones [38, 39].

#### **Anthelmintic activity**

It has shown significant anthelmintic activity in various studies, primarily due to its bioactive compounds, including cardiac glycosides, flavonoids, and saponins. Traditionally, parts of the plant, such as leaves, seeds, and bark, have been used in small doses to treat parasitic worm infections. The anthelmintic effects of *Thevetia peruviana* are attributed to its toxic compounds, which can interfere with the physiological processes of helminths, leading to their expulsion or death. The cardiac glycosides, especially thevetin A and thevetin B, have been identified as key contributors to the plant's anthelmintic properties. These compounds are known to disrupt the cellular mechanisms of helminths by inhibiting essential enzymes or altering their cellular homeostasis [40, 41].

#### **Pesticidal activity**

Several studies have focused on the pesticidal effects of *Thevetia peruviana* extracts, revealing promising results. The plant's seed extract, in particular, has been shown to exhibit potent insecticidal activity against a range of agricultural pests. The action of these extracts often targets the nervous system of insects, leading to paralysis and death. In laboratory

experiments, *Thevetia peruviana* extracts have successfully controlled pests such as the red flour beetle, housefly larvae, and cotton bollworm. These pests are significant threats to agricultural productivity, and the use of plant-derived pesticides offers a safer, environmentally friendly alternative to synthetic chemicals [42].

#### **CONCLUSION**

In conclusion, *Thevetia peruviana* (yellow oleander) is a plant with both toxic and therapeutic potential. Its complex phytochemical profile, rich in cardiac glycosides, alkaloids, flavonoids, and other bioactive compounds, underpins its significant pharmacological effects, including anti-inflammatory, antimicrobial, antidiabetic, anticancer, and antioxidant properties. However, the plant's toxicity, particularly due to the presence of potent cardiac glycosides, poses a major challenge for its safe use in medicine.

Pharmacokinetic and molecular studies have provided valuable insights into the absorption, distribution, metabolism, and elimination of its active compounds, as well as their mechanisms of action at the cellular level. This research is crucial for identifying safe and effective dosages and delivery methods, ensuring that the therapeutic benefits of *Thevetia peruviana* can be harnessed while minimizing the risk of poisoning.

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