Review Article

Plumbago Zelyanica Linn. (Chitraka) Under the Lens; A Research Review Study of Overall Plant Toxicity, Phytotoxic Impacts and Ecological Consequences

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ABSTRACT

Background: *Chitraka*, (Plumbago zeylanica) is a widely used medicinal plant in India, employed in various traditional systems such as Ayurveda. Despite its therapeutically valuable bioactive compounds, the plant is associated with marked toxicity and phytotoxicity in both experimental models and clinical usage. Objectives: To systematically review and synthesize the existing scientific evidence on the overall toxicity and phytotoxicity of Plumbago zeylanica, with a focus on human, animal, and plant models within the Indian context. Methods: A comprehensive literature review was conducted using subject specific, multi-disciplinary and electronic databases with official guidelines. Inclusion criteria were original studies, reviews, and case reports published in English up to 2024 dealing with acute, sub-acute, and chronic toxicity, as well as phytotoxicity of *Plumbago zeylanica*, particularly from Indian mainland. Extraction focused on toxicological endpoints, affected organs, dose-response relationships, and mechanisms.

Results: Studies consistently identify plumbagin, a naphthoquinone, as the principal toxic constituent, exhibiting potent cytotoxic and pro-oxidant activities. Animal studies demonstrate pronounced acute and sub-acute toxicity, with hepatic and renal impairment, haematological changes, and increased organ masses at higher doses. LD50 values show petroleum ether extracts as more toxic than acetone or hydroalcoholic extracts (*LD50: 93.45 mg/kg vs. 928.4 mg/kg*). Clinical reports detail gastrointestinal, cardiac, neurological, and dermatological toxic manifestations with high or improper dosage. Phytotoxicity is observed in soil and allelopathic studies, affecting

germination and growth of other plants. Misuse as an abortifacient and to produce bruises (for malingering) has medicolegal significance in India.

Conclusion: Plumbago zeylanica poses significant risks due to its toxicity and phytotoxicity. Awareness and regulatory measures are vital to minimize adverse outcomes associated with its traditional and modern therapeutic use.

Keywords: *Plumbago zeylanica, plumbagin, phytotoxicity, toxicity, herbal medicine, hepatic toxicity, allelopathy, medicinal plants.*

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INTRODUCTION

Chitraka commonly known as Ceylon leadwort with botanical name Plumbago zeylanica Linn. (family: Plumbaginaceae), is prevalent in India's traditional medicine for treating multiple ailments, including inflammation, digestive disorders, and cancer. Despite its therapeutic benefits, growing evidence underscores considerable toxicity associated with various extracts and phytoconstituents, chief among them plumbagin, a naphthoquinone with documented cytotoxic and genotoxic effects. Reports of adverse effects, ranging from mild gastrointestinal upsets to severe hepatic and renal injury, and cases of deliberate poisoning or medico-legal misuse, necessitate a critical appraisal of its safety profile. Moreover, the plant displays notable phytotoxic (allelopathic) activity, impacting agricultural ecosystems[1].

Given India's continued reliance on herbal and herbo-mineral medicine, it is vital to systematically evaluate the scientific evidence regarding both overall toxicity and phytotoxicity of Plumbago zeylanica. This review aims to provide a comprehensive, evidence-based synthesis for clinicians, toxicologists, researchers, and policymakers.

MATERIALS AND METHODS

Strategy

A systematic literature search was conducted using subject specific, multi-disciplinary and electronic databases with official guidelines. Additional grey literature, traditional pharmacopoeias, and regulatory guidelines were consulted.

Inclusion/Exclusion Criteria

Studies included original research articles, reviews, experimental animal studies, clinical reports, case series, and allelopathy studies directly addressing the toxicity or phytotoxicity of Plumbago zeylanica, with a geographical preference for Indian data or context. Exclusions were non-peer-reviewed sources, conference abstracts without full data, and studies lacking explicit toxicological endpoints.

Data Extraction and Synthesis

Data were extracted for plant part used, extraction method, test system (animal, plant, clinical), dosage, duration, observed toxic effects, biochemical and histological findings, phytochemical constituents (primarily plumbagin), and proposed mechanisms. Both qualitative and quantitative results were collated and critically analyzed.

Quality Assessment

Studies were evaluated for methodological rigor using guidelines similar to the ARRIVE criteria for animal studies and PRISMA for review articles, focusing on study design, sample size, controls, and outcome measures.

Review of Literature

1. Toxic Constituents and Phytochemistry

Plumbago zeylanica is rich in secondary metabolites, especially plumbagin, which constitutes the primary toxic principle. Other notable compounds include various flavonoids, triterpenoids, and alkaloids. Plumbagin exhibits strong redox cycling and pro-oxidant effects, accounting for its bioactivity and toxicity. Plumbagin is particularly noted for its pharmacological potency (antimicrobial, anticancer, and antifertility actions). Homoeopathic indications generally centre on digestive complaints like diarrhoea, flatulence, peptic ulcer, and are extended to chronic conditions due to its immunosuppressive and anti-inflammatory effects[7]. Plumbago zeylanica being a powerful irritant; the roots and leaves contain compounds that can cause skin blistering and are abortifacient in large doses, so safety and dosing precautions are critical[5]. It's purified and often employed in low doses for its digestive, immunomodulatory, and anti-infective properties, but traditional use also covers cardiovascular, hepatic, and metabolic disorders [3][7]. The plant can be toxic in higher doses, causing blisters and systemic toxicity, and its abortifacient effects are well documented; traditional ayurvedic and homeopathic practitioners must apply great caution[2][5][7].

2. Toxicity in Animal Studies

Numerous animal studies report acute and sub-acute toxicities, primarily in rodent models. Petroleum ether extracts are reported as the most toxic (LD50: 93.45 mg/kg), with acetone and hydroalcoholic extracts much less so (LD50: 928.4 mg/kg). Dose-dependent hepatic and renal lesions, hematological changes (anemia, leukopenia), and elevated serum enzymes (AST, urea, creatinine) have been consistently observed. Chronic exposure also affects cardiac and adrenal weights, indicating systemic toxicity. Disturbingly, these extracts are not traditionally used, but their study demonstrates the risks associated with specific phytoconstituent enrichment[3].

3. Clinical and Medico-legal Reports

Traditional use in India as an abortifacient and for therapeutic abortion has resulted in

cases of toxicity and, rarely, fatalities. Symptoms include abdominal pain, emesis, red and itchy skin, dilated pupils, myotonia, CNS depression, hypotension, arrhythmias, and respiratory failure. Overdose or misuse leads to severe outcomes, while topical application is linked to dermal irritation and artificial bruising for forensic malingering[4]. It is also used in homoeopathy and is recognized for its broad pharmacological properties including antibacterial, anti-inflammatory, anticancer, antioxidant, antifungal, and wound-healing effects

4. Phytotoxicity and Allelopathic Effects

Allelopathic (phytotoxic) influences of Plumbago zeylanica have been recognized in controlled experiments, with significant inhibition of seed germination and growth in neighboring plants. This effect is attributed to root exudates and leached naphthoquinones, which can alter soil microflora and agricultural productivity in areas where the plant grows prolifically [5].

RESULTS

1. Acute and Sub-Acute Toxicity in Experimental Models

1.1 Petroleum Ether, Acetone, and Hydroalcoholic Extracts

Animal studies repeatedly demonstrate that petroleum ether extracts of Plumbago zeylanica root are the most acutely toxic, with observed LD50 values as low as 93.45 mg/kg in murine models. In contrast, hydroalcoholic and acetone extracts present less acute toxicity, with LD50 values exceeding 900 mg/kg. Sub-lethal dosages frequently produce notable histopathological alterations in liver and kidney tissue, including hepatocyte necrosis, centrilobular swelling, tubular degeneration, and glomerular atrophy. Observation periods ranging from 7 to 28 days reveal progressive pathology, with biochemical assays confirming marked elevations in serum transaminases (AST, ALT), ALP, and renal markers (serum creatinine and urea) [3,6].

1.2 Hematological Toxicity

Subacute exposure (14–28 days, repeated dosing) leads to pronounced hematological changes—anemia, leukopenia, and, in some studies, thrombocytopenia. These alterations are dose-dependent and correlate with suppression of bone marrow activity or direct cytotoxicity to hematopoietic cells, as confirmed by histological examination of femoral marrow [7].

1.3 Chronic and Developmental Toxicity

Chronic exposure studies (up to 90 days) detail hypertrophy in the liver, kidneys, adrenals, and heart. Toxic manifestations extend to reproductive toxicity, with higher rates of fetal resorption and abortion in pregnant animal models. Plumbagin passes readily through placenta and is implicated in embryotoxic and teratogenic effects; exposure during gestation correlates with

delayed organogenesis and malformations[8].

2. Clinical Toxicity and Reported Adverse Events

2.1 Human Case Reports and Traditional Use

Adverse effects in humans, documented in both case reports and clinical observations, mirror findings in preclinical models. Purging, vomiting, abdominal pain, dermatitis, CNS depression, arrhythmias, and hypotension are predominant. Traditional use as an abortifacient among rural populations remains prevalent, and although rare, severe poisonings and fatalities have been documented. Misidentification, overdose, and wrongful substitutions exacerbate risks, particularly when roots are marketed or self-administered due to folk remedies.[8,9]

2.2 Medicolegal Abuse

Plumbago zeylanica roots have historically been applied externally to induce blisters and simulate bruising for medicosocial gain—i.e., malingering or feigning injury—a practice still occasionally noted in forensic medicine reports from northern and eastern India[10].

3. Phytotoxic and Allelopathic Effects

3.1 Laboratory and Field Trials

Extracts from Plumbago zeylanica—especially root and leaf aqueous and ethyl acetate fractions—are potently inhibitory to seed germination and seedling growth of crop species such as rice (Oryza sativa), wheat (Triticum aestivum), and cucumber (Cucumis sativus). Germination rates drop by 40–70% upon soil amendment with increasing concentrations of Plumbago extracts, and root elongation suffers even at low doses (0.01–0.1% w/v). Field studies in India's Gangetic plains further reveal that dense stands of wild Plumbago zeylanica depress crop yields through allelopathic suppression and soil microbial shifts[10,11].

3.2 Soil Microbial Interactions

Soil samples from Plumbago zeylanica-dense areas highlight reductions in fungal and bacterial counts, indicating the release of bioactive exudates with broad-spectrum phytotoxic and antimicrobial activity. This disrupts rhizospheric balance, plant succession, and is detrimental to non-target crops and soil health[12].

4. Mechanisms of Toxicity

4.1 Plumbagin and Oxidative Stress

The naphthoquinone plumbagin is recognized as the chief toxic principle, exerting cytotoxicity via:

- Free radical generation (ROS/RNS)
- Lipid peroxidation of cell membranes
- Mitochondrial dysfunction and ATP depletion
- DNA fragmentation and apoptosis/necrosis induction
- Inhibition of cellular antioxidant enzymes (SOD, catalase, GSH-peroxidase)[13]

4.2 Synergy with Other Phytochemicals

Other bioactive constituents (flavonoids, alkaloids) may amplify toxicity via synergistic or additive effects on cell cycle arrest, DNA binding, and protein cross-linking[13].

Discussion

1. Contextualizing Toxicity of Plumbago zeylanica in Indian Traditional Medicine

Plumbago zeylanica occupies a paradoxical position in India's healers' pharmacopeia: revered as a potent "rasayana" and yet shadowed by a history of adverse outcomes. Ayurvedic and Siddha practitioners have long stressed the need for careful dose adjustment and purification (shodhana) of "chitrak" roots prior to use. However, scientific scrutiny reveals that improper processing, accidental overdosing, or unsupervised use can have grave consequences[14].

2. Risks of Traditional and Folk Usage

Despite official warnings and increasing regulatory oversight, rural and semi-rural populations in India continue to access and use raw Plumbago zeylanica material for purposes ranging from digestive complaints to fertility regulation. The margin between therapeutic and toxic dose is narrow, particularly for roots containing high concentrations of plumbagin—often exceeding 0.3% dry weight. Weak regulation in markets, incomplete implementation of herbal guidelines, and widespread misconceptions about "natural" safety heighten risks of poisoning events[15].

3. Implications for Human and Animal Health

Systemic toxicity in animal studies—hepatic, renal, hematological, and cardiac injury—provides plausible bases for similar risks in humans. Plumbagin's low oral LD50, broad pro-oxidant activity, and its known effects in inhibiting DNA repair mechanisms render it particularly hazardous in vulnerable populations (children, pregnant women, elderly). Chronic exposure, whether intentional or environmental, may contribute to kidney and liver disease burden in populations with high "chitrak" consumption or those living around wild stands[16].

4. Medicolegal and Socioeconomic Consequences

The plant's misuse in traditional abortifacient practices presents a unique medico-legal challenge in India. Several reports document self-administered or otherwise clandestine ingestion of Plumbago zeylanica for abortion, with resultant morbidity and, on occasion, mortality. Forensic pathologists must maintain high suspicion in unclear cases of hepatic or renal collapse in reproductive-age women from communities where the practice is known.

The use of the plant to simulate bruising or injury ("quack" malingering) also poses diagnostic and legal complications,

potentially undermining judicial processes and compensation claims[17].

5. Ecological Impact due to Phytotoxicity

The allelochemicals released from Plumbago zeylanica have direct and deleterious effects on agricultural systems. Crop suppression, reduced germination, and shifts in soil biota are well documented. Not only does this threaten food security at the local and regional level—in subsistence and small-holder agriculture, especially—but it can alter ecosystem structure, promoting invasive potential and hindering natural succession.

The ecological footprint of Plumbago zeylanica is underestimated, as adverse effects extend beyond the plant itself to enrich the competitive advantage of wild conspecifics while suppressing economically important crops[18].

6. Mechanistic Insights and Pharmacovigilance

The toxicodynamics of plumbagin and related naphthoquinones illustrate the perils of assuming herbal panaceas are automatically safe. Plumbagin's calcineurin inhibition, electrophilic attack on nucleic acids, and its ability to trigger apoptotic pathways underscore a need for strict dosage control and public education.

Systemic, well-designed pharmacovigilance programs—currently lacking in indigenous herbal safety monitoring—are needed. Outreach to traditional practitioners, standardization of herbal formulations, and enforcement of labeling laws should be prioritized[19].

7. Gaps in Current Knowledge and Future Directions

Despite growing interest, several knowledge gaps remain:

- Large-scale, controlled clinical toxicity trials in Indian populations are lacking.
- Long-term ecological studies on allelopathic build-up and mitigation strategies are limited.
- Toxicogenomic, metabolomic, and proteomic analyses for human/plants are sparse.
- No standardized guidelines exist for acceptable exposure limits in medicinal or environmental contexts.

Future research must target these gaps, focusing on better characterization of constituent toxicity, safe processing protocols, and the ecological ramifications in diverse agricultural systems [20].

CONCLUSION

Plumbago zeylanica (Ceylon leadwort) is an indigenous medicinal plant of great significance in Indian traditional medicine systems. While its potent phytoconstituents, especially plumbagin, underpin a wide array of purported therapeutic effects, converging scientific and clinical evidence clearly highlights substantial risks of toxicity and phytotoxicity.

Experimental studies elucidate that extracts, particularly petroleum ether fractions, can induce marked hepatic, renal, and haematological damage in animal models. Human case reports confirm such adverse effects, especially in the setting of misuse, overdose, or unsupervised self-administration. The plant has a notorious history of medico-legal misuse—including as an abortifacient and for malingering—adding to its risk profile. In the agro-ecological context, Plumbago zeylanica's allelopathic activity disrupts seed germination and crop viability, underlining its status as both a pharmacological resource and an agricultural hazard.

Regulatory and educational interventions are thus urgently needed. Standardization of herbal preparations, strict labelling, and effective outreach to folk practitioners can help reduce accidental poisonings. Modern pharmacovigilance systems, integration of traditional knowledge with toxicological assessment, and long-term ecological monitoring will ensure safer use of this plant. Further research, especially population-based clinical studies and mechanistic analyses, is warranted to delineate safe exposure limits and sustainable utilization strategies. Balancing Plumbago zeylanica's valuable medicinal potential against its tangible toxicity and ecological risks remains an essential challenge for researchers, clinicians, and policymakers in India.

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