Toxicology Risk Summary - Guduchi (Tinospora Cordifolia)

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Abstract- Guduchi (*Tinospora cordifolia*), a revered herb in Ayurvedic medicine, has long been celebrated for its immunomodulatory, hepatoprotective, and adaptogenic properties. This technical dossier presents a comprehensive evaluation of Guduchi's therapeutic potential, safety profile, and pharmacological actions, especially in light of recent concerns regarding its hepatotoxicity. Drawing from classical Ayurvedic texts, modern pharmacological studies, and clinical trials, the document critically assesses both the benefits and risks associated with Guduchi. It concludes that, when properly identified and administered, *T. cordifolia* remains a safe and efficacious herb for a wide range of health conditions, including infectious diseases, autoimmune disorders, and metabolic syndromes. The dossier also emphasizes the importance of botanical authentication and standardized formulations to ensure safety and efficacy.

Keywords- Tinospora cordifolia, Guduchi, Ayurvedic medicine, Immunomodulation, Hepatoprotection, Rasayana, Herb-induced liver injury (HILI), Autoimmune hepatitis, Phytochemistry, Clinical trials, Toxicology

1.0 INTRODUCTION

Tinospora cordifolia (Willd.), commonly known as Guduchi, Giloy, or Amritavalli, is a deciduous climbing shrub belonging to the Menispermaceae family. Native to tropical and subtropical regions of Asia, it is characterized by succulent stems, heart-shaped leaves, and red drupe fruits. In Ayurveda, Guduchi is revered as a Rasayana herb—an agent that rejuvenates, enhances vitality, and promotes longevity. Its Sanskrit epithet "Amritavalli" reflects its status as the "nectar of immortality."

Historically referenced in classical texts such as the Charaka Samhita and Sushruta Samhita, Guduchi has been employed for over 3,000 years in the treatment of fever, jaundice, diabetes, skin disorders, and chronic fatigue. Its therapeutic versatility is attributed to a rich phytochemical profile, including alkaloids (e.g., tinosporine), glycosides, terpenoids, flavonoids, and polysaccharides. These constituents confer a wide range of pharmacological actions—antipyretic, anti-inflammatory, antioxidant, immunomodulatory, and hepatoprotective.

Modern research has validated many of these traditional claims, with studies highlighting Guduchi's role in modulating immune responses, protecting hepatic tissues, and improving insulin sensitivity. Its widespread use during the COVID-19 pandemic further underscores its relevance in contemporary integrative medicine. As such, Tinospora cordifolia continues to bridge ancient wisdom with modern biomedical inquiry.

2.0 ETHNOMEDICINAL USES

Tinospora cordifolia, commonly known as Guduchi or Giloy, has been extensively utilized in traditional medicine systems across South Asia for its broad therapeutic spectrum. Ethnomedicinal practices highlight its role in managing febrile conditions, metabolic disorders, and immune dysfunctions. dangerous condition, kernicterus (brain damage due to high bilirubin levels).

Berberine can also pass through the breast milk during breastfeeding to which the newborn baby is exposed. And because the liver enzymes of the newborn are still immature, there is a problem in the metabolism of the drug and the chance of toxicity is very high.

3.0 PHYTOCHEMICAL COMPOSITION

Tinospora cordifolia (Guduchi) is a rich reservoir of bioactive compounds that contribute to its wide-ranging therapeutic potential. Phytochemical investigations have revealed the presence of diverse classes of constituents, including alkaloids, glycosides, terpenoids, steroids, and polysaccharides.

Key Bioactive Compounds

- Alkaloids: Berberine, magnoflorine, tembetarine, choline
- Glycosides: Tinosporaside, cordifolioside A, cardiofoliosides A &B
- Terpenoids: Diterpenoid furanolactones such as tinosporide, tinosporidine, and columbin
- Steroids: β-sitosterol, giloin, giloinisin
- Phenoliclignans: Aryltetrahydrofuranolignan and others with antioxidant properties

Quantitative Highlights

- Cordifolioside A: ≥ 0.02% w/w
- Tinosporaside: 0.03–0.04%
- Macronutrient profile: High carbohydrate (61.66%), moderate protein (4.5–11.2%), low fat (3.1%)
- Mineral content: High potassium (0.845%), chromium (0.006%), iron (0.28%), calcium (0.131%)

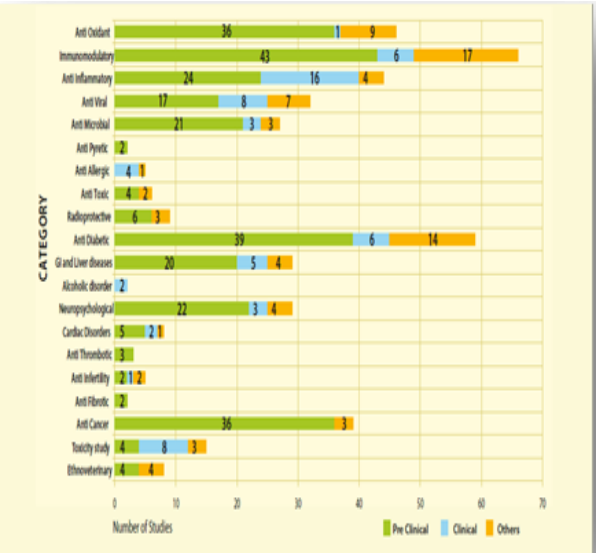

Figure.1. Categorization of articles based on the condition/effect studied

4.0 PHARMACOLOGICAL PROPERTIES

tinospora cordifolia (Guduchi) exhibits a broad spectrum of pharmacological activities, validated through both traditional Ayurvedic use and modern biomedical research. Its bioactive constituents—particularly alkaloids, glycosides, and flavonoids—contribute to its therapeutic versatility.

Core Pharmacological Actions

- Immunomodulatory: Guduchi enhances innate and adaptive immunity by stimulating macrophage activity, increasing IL-2 levels, and suppressing pro-inflammatory cytokines like TNF-α.
- Antioxidant: Rich in phenolics and flavonoids, it scavenges reactive oxygen species, elevates antioxidant enzymes (SOD, catalase), and reduces lipid peroxidation markers such as malondialdehyde (MDA).
- Anti-inflammatory & Analgesic: Extracts inhibit COX-2 and NF-κB pathways, reducing inflammation and pain in models of edema and nociception, comparable to standard NSAIDs.
- Antipyretic: Guduchi decoction modulates hypothalamic thermoregulation, effectively lowering fever in experimental models—aligning with its classical *Jwarahara* (fever-reducing) role.
- Antidiabetic: Demonstrates significant glucose-lowering effects in streptozotocin and alloxan-induced models, improves pancreatic β-cell histology, and inhibits aldose reductase (IC_{50} ≈ 103 µg/mL).
- Hepatoprotective: Restores liver enzyme levels (ALT, AST, ALP) and bilirubin in CCl_4-induced injury, while boosting hepatic glutathione and reducing oxidative stress.
- Antimicrobial: Shows activity against *Staphylococcus aureus* and *E. coli*, and inhibits viral replication in vitro, possibly via interference with viral polymerases.
- Anti-osteoporotic: Prevents bone loss in ovariectomized rats by enhancing osteocalcin and inhibiting osteoclastogenesis, suggesting potential in postmenopausal osteoporosis.
- Anticancer & Antimalarial: Exhibits cytotoxicity against breast and colon cancer cell lines via

apoptosis induction; alkaloids inhibit plasmodial enzymes in malaria models.

- Neuroprotective & Wound Healing: Improves memory retention in murine models and accelerates wound contraction and collagen synthesis, supporting its nootropic and regenerative roles.

5.0 MECHANISMS OF ACTION

- Modulates both innate and adaptive immunity via macrophage activation, T-cell stimulation and cytokine regulation (IL-6, TNFα).
- Exhibits COX-2 and iNOS inhibition, dampening inflammatory cascades.
- Scavenges free radicals and up-regulates antioxidant enzymes (SOD, catalase) to protect against oxidative injury

6.0 HEPATIC EFFECTS

- Reverses CCl_4-, paracetamol- and alcohol-induced liver damage in rodents by normalizing transaminases, bilirubin and histology.
- Enhances Kupffer-cell clearance of toxins and preserves mitochondrial integrity in hepatocytes.

7.0 RENAL IMPACT

- Attenuates gentamicin- and aflatoxin-induced nephrotoxicity in rats by stabilizing glomerular structures and reducing lipid peroxidation.
- Improves renal antioxidant status and promotes tissue repair in acute kidney-injury models.

8.0 CYTOTOXICITY PROFILE

- Non-mutagenic in bacterial Ames assays up to 5 mg/plate and non-clastogenic in lymphocyte cultures up to 3 mg/mL.
- No DNA damage in mouse bone-marrow micronucleus or comet assays at doses ≤ 250 mg/kg.

9.0 DOSE – RESPONSE RELATIONSHIP

- Safe and effective in preclinical models at 100–1,000 mg/kg/day.
- Clinical doses range 500 mg–2 g/day in adults; decoctions typically use 10–30 g raw stem.

10. NOAEL & LD_{50} DATA

- No observable adverse effect level above 1 g/kg in rodents.
- Oral LD_{50} estimated > 2 g/kg in mice, indicating low acute toxicity.

11. PREPARATION METHODS

- Decoction (Kwatha): stem boiled in water until reduced to 1/8th.
- Cold infusion (Hima), fresh juice (Swarasa), powder (Churna), and various oil/ghee preparations.
- Standardized extracts (aqueous, hydro-ethanolic or chloroform) enriched in marker compounds (tinosporaside, cordifolioside A).

12. HERB-DRUG INTERACTIONS

- Weak inhibition of major CYP450 isozymes (CYP3A4, 2D6, 2C9, 1A2) at high concentrations; unlikely to cause clinically relevant interactions.

13. CASE STUDIES & REPORTS

- Millions have used it safely for centuries; recent COVID-19 add-on trials report no serious liver or kidney adverse events.
- Rare case series of liver injury lacked definitive causality (often involved polyherbal mixes, pre-existing disease, or misidentified species).age

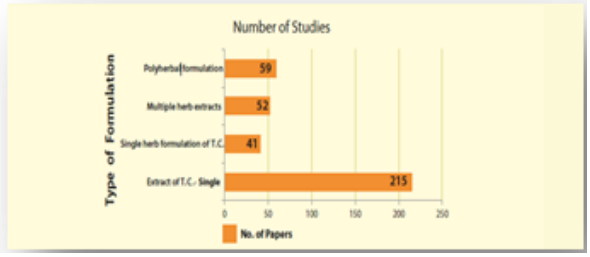

Figure.2. Categorization of articles based on the type of formulation/intervention used

14. REGULATORY & SAFETY GUIDELINES

- Included in the Ayurvedic Pharmacopoeia of India with limits on foreign matter (≤ 2 %), ash (total ≤ 16 %), and extractives.
- Ministry of AYUSH advisory emphasizes correct species authentication an compliance with pharmacopoeial standards.

15. CONCLUSION & RECOMMENDATIONS

- Tinospora cordifolia demonstrates broad organ protection and immunomodulation with a wide safety margin.
- Future work should clarify long-term use, herb–drug synergy and species authentication to ensure consistent quality and minimize risk.

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