

THERAPEUTIC POTENTIAL AND TOXICOLOGICAL RISKS OF SELECTED TOXIC MEDICINAL PLANTS: A PHARMACOGNOSTIC AND ETHNOPHARMACOLOGICAL REVIEW

Dimitri Kochadze MD¹

Elguja Latchkepani MD²

Robert Makharashvili MD³

Dimitri Kutchukhidze MD⁴

¹ Infectious Disease Physician, PhD student of Tbilisi State Medical University, Assistant of Histology, International School of Medicine, Alte University
Orcid ID: <https://orcid.org/0009-0009-9976-4724>

² Levan Samkharauli National Forensic Bureau, Department of Medical Examination Department, Forensic Medical Expert at Living Bodies and Corpses Examination Unit;

PhD student of Tbilisi State University Georgia
Orcid ID: <https://orcid.org/0000-0002-6639-7595>

³ Givi Zhvania Pediatric University Clinic of Tbilisi State Medical University, Anesthesiologist, Critical Care Physician (Anesthesiology and Critical Care)
Orcid ID: <https://orcid.org/0009-0000-5849-9340>

⁴ Anesthesiologist, National Center of Otorhinolaryngology - Japaridze-Kevanishvili Clinic, Tbilisi, Georgia;
Anesthesiologist and Critical Care Physician, American Hospital Tbilisi, Georgia;
Lecturer, David Tvildiani Medical University, Tbilisi, Georgia

Abstract

Toxic medicinal plants occupy a complex position at the interface of pharmacognosy, ethnopharmacology, clinical pharmacology, and toxicology because the same secondary metabolites that provide potentially useful biological activity may also cause severe or fatal poisoning. This narrative review evaluates seven toxic medicinal plants that represent different pathways from traditional use to contemporary pharmaceutical relevance: *Hyoscyamus niger* L., *Veratrum album* L. (syn. *V. lobelianum* Bernh.), *Ricinus communis* L., *Rauvolfia serpentina* (L.) Benth. ex Kurz, *Physostigma venenosum* Balf., *Podophyllum peltatum* L., and *Rhododendron ponticum* L. The review integrates six source books supplied for the study, including Georgian medicinal-plant, historical, and geobotanical literature together with major international herbal monographs, and supplements them with peer-reviewed pharmacological, clinical, and toxicological evidence. For each species, botanical and pharmacognostic characteristics, historical and ethnopharmacological use, principal active or toxic constituents, mechanisms of action, modern therapeutic development, and safety

limitations were compared. The analysis demonstrates several distinct translational models: isolation of active alkaloids such as scopolamine, reserpine, and physostigmine; processing that separates a medicinal product from a hazardous plant constituent, as in castor oil and ricin; semisynthetic drug development from podophyllotoxin; and species such as *Veratrum* and *Rhododendron* whose contemporary significance is predominantly toxicological. The findings emphasize that historical use and pharmacological activity are not equivalent to clinical efficacy. Safe therapeutic translation requires authenticated botanical material, chemical characterization, standardization, controlled dosing, clinical evaluation, and toxicological surveillance.

Keywords: toxic medicinal plants, pharmacognosy, ethnopharmacology, alkaloids, plant toxins, pharmacotherapy, toxicology, drug discovery, safety.

Introduction

Medicinal plants have contributed to healthcare for millennia, but their historical importance also demonstrates that natural origin is not synonymous with safety. Pharmacologically active plant metabolites evolved primarily for ecological functions and may interact with human receptors, enzymes, ion channels, structural proteins, or nucleic acids with sufficient potency to generate both therapeutic effects and severe toxicity. This relationship is especially evident among plants rich in tropane alkaloids, steroidal alkaloids, indole alkaloids, lignans, diterpenoids, and toxic proteins. Major herbal reference works therefore distinguish between traditional use of a crude plant and modern use of an isolated, standardized, or chemically modified constituent (Gruenwald et al., 2007; Duke et al., 2002; Chevallier, 2016).

The Georgian pharmacognostic literature treats toxic plants as a distinct medicinal category and specifically includes *Hyoscyamus niger* and *Veratrum lobelianum* among poisonous medicinal species. It also emphasizes that the biological activity of medicinal raw material is influenced by the plant organ, developmental stage, environmental conditions, harvesting, drying, and processing (Bidzinashvili & Eradze, 2021). Georgian historical sources document the long-standing use of plant-derived products in the territory of Georgia, while geobotanical literature demonstrates the exceptional floristic diversity of the country and the persistence of relict elements such as *Rhododendron ponticum* within the Colchic vegetation complex (Melikishvili, 1970; Kvachakidze, 2009). These historical and geographical observations are important for ethnopharmacological context, but they do not by themselves establish modern therapeutic efficacy.

Recent Georgian scholarship has increasingly framed traditional medicinal knowledge as a subject for systematic pharmacognostic and ethnopharmacological research rather than as a set of uncritical therapeutic instructions. Studies by Kochadze and colleagues have examined the historical foundations of Georgian ethnopharmacology, medicinal-plant cultivation practices and knowledge transmission, medicinal geophytes, the development of herbalism from early traditional systems toward scientific medicine, and the pharmacognostic significance of selected plants from Khvamli Mountain (Kochadze, Latchkepani, & Makharashvili, 2025; Kochadze et al., 2025a, 2025b; ჯიჭაძე et al., 2026). This approach is particularly relevant to toxic

medicinal plants, where a historically observed effect may be biologically real while the crude preparation remains unsuitable for contemporary clinical use.

The transition from poisonous plant to medicine can follow several paths. A toxic botanical source may yield an isolated pharmaceutical compound, as occurred with scopolamine from tropane-alkaloid-producing Solanaceae, reserpine from Rauvolfia, and physostigmine from Physostigma. Processing may remove or exclude the dangerous constituent while preserving a useful medicinal fraction, as in pharmaceutical castor oil versus ricin-containing seed material. A natural molecule may also serve as a medicinal-chemistry scaffold, illustrated by podophyllotoxin and the subsequent development of epipodophyllotoxin derivatives. Conversely, some historically used plants remain predominantly toxicological subjects because their chemical variability and narrow therapeutic margins outweigh their potential clinical benefit. The seven species selected for the present review were chosen to illustrate these contrasting trajectories.

Aim and Objectives of the Study

The aim of this study was to provide a comparative pharmacognostic and ethnopharmacological assessment of seven selected toxic medicinal plants and to evaluate how their historical uses, chemical constituents, mechanisms of action, pharmaceutical development, and toxicological risks relate to contemporary medicine. The objectives were to: (1) identify the medicinally important plant parts and principal bioactive or toxic constituents; (2) summarize documented traditional and historical uses without treating them as evidence of efficacy; (3) describe molecular or cellular mechanisms where supported by modern research; (4) distinguish crude plant use from purified, standardized, processed, or semisynthetic pharmaceutical products; (5) compare characteristic poisoning syndromes and safety limitations; and (6) integrate Georgian pharmacognostic and geobotanical context where directly supported by the supplied sources.

The study was conducted as a source-based narrative review. Six supplied books formed the core reference base: Samkurnalo mcenareebis kultura [Medicinal Plant Cultivation] (Bidzinashvili & Eradze, 2021), Vegetation of Georgia (Kvachakidze, 2009), Essays on the History of Georgia, Volume I (Melikishvili, 1970), PDR for Herbal Medicines (Gruenwald et al., 2007), Handbook of Medicinal Herbs (Duke et al., 2002), and Encyclopedia of Herbal Medicine (Chevallier, 2016). Historical and geobotanical texts were used for contextualization, whereas plant-specific pharmacology and toxicology were based primarily on pharmacognostic monographs and contemporary peer-reviewed research. Additional clinical, analytical, and mechanistic studies were incorporated to verify current evidence, particularly where modern medicine uses an isolated constituent rather than the crude plant. Historical dosage descriptions were not converted into contemporary recommendations because toxin concentrations may vary substantially by species, organ, chemotype, growth conditions, and preparation method.

Research Results and Discussion

All seven species demonstrate that the terms “medicinal” and “toxic” are not mutually exclusive. Their relationship depends on botanical identity, chemical

composition, dose, route of administration, plant organ, processing, and whether the therapeutic intervention consists of crude material or a chemically defined product. The Georgian medicinal-plant source explicitly notes that powerful plant poisons may become sources of medicinal substances when active constituents are isolated and used under controlled conditions (Bidzinashvili & Eradze, 2021). The following species illustrate different pharmacognostic models of this principle.

***Hyoscyamus niger* L. - Henbane**

Hyoscyamus niger is an annual or biennial member of the Solanaceae. The medicinal raw material has historically consisted mainly of the leaves and flowering aerial parts, although seeds and roots also contain pharmacologically important tropane alkaloids. Georgian pharmacognostic literature lists henbane among poisonous medicinal plants, while Chevallier and Duke describe a long record of use for pain, gastrointestinal spasm, respiratory symptoms, insomnia, and other conditions (Bidzinashvili & Eradze, 2021; Chevallier, 2016; Duke et al., 2002). These uses are understandable in light of antimuscarinic pharmacology, but historical indications should not be interpreted as contemporary recommendations.

The principal constituents are hyoscyamine and scopolamine (hyoscine), accompanied by related tropane alkaloids. Modern analytical work confirms that concentrations vary substantially among plant organs and samples. Ahmadpour et al. (2024) quantified both hyoscyamine and scopolamine in *H. niger* roots, illustrating the importance of plant organ, provenance, extraction, and analytical method. Such variability is a central pharmacognostic problem because crude botanical material cannot reliably reproduce the exposure achieved with a standardized pharmaceutical preparation. The major pharmacodynamic mechanism is competitive antagonism of muscarinic acetylcholine receptors. Peripheral effects include reduced secretion, inhibition of smooth-muscle activity, mydriasis, and tachycardia; central effects may include sedation at controlled exposure and agitation, hallucinations, delirium, or seizures in poisoning.

Contemporary therapeutic relevance belongs principally to purified tropane alkaloids rather than to henbane itself. Scopolamine is used as a standardized pharmaceutical antimuscarinic, while *H. niger* also remains of interest as a biosynthetic source for tropane alkaloids. The distinction is critical: evidence supporting pharmaceutical scopolamine cannot be transferred to teas, powders, tinctures, or other crude henbane preparations. The classical antimuscarinic toxidrome includes dry mucosae, mydriasis, tachycardia, urinary retention, impaired sweating, hyperthermia, agitation, confusion, hallucinations, and in severe cases seizures and systemic complications. Recent pediatric intensive-care data confirm that severe exposure may be associated with seizures and other complications despite generally favorable outcomes with appropriate supportive care (Terzi et al., 2026). Thus, *H. niger* exemplifies a plant whose pharmaceutical importance survives primarily through isolated, standardized constituents.

***Veratrum album* L. (syn. *V. lobelianum* Bernh.) - White Hellebore**

Veratrum species are perennial monocotyledonous plants with rhizomes and roots that contain a complex mixture of steroidal alkaloids. The Georgian source records

Veratrum lobelianum under the local name shkhama and identifies the rhizome with roots as medicinal raw material (Bidzinashvili & Eradze, 2021). Historical uses included emetic, analgesic, antiparasitic, external, and hypotensive applications. Duke and PDR, however, place particular emphasis on the plant's toxicity and narrow safety margin (Duke et al., 2002; Gruenwald et al., 2007). Modern chemistry confirms that this is not a single-compound plant: protoveratrine, veratridine, cevadine, jervine, veratramine, and numerous related alkaloids may be present in different proportions.

The pharmacology of *Veratrum* is closely related to disruption of excitable membranes. Veratridine-type alkaloids interact with voltage-gated sodium channels and interfere with normal inactivation, promoting persistent sodium conductance and abnormal depolarization. This provides a mechanistic explanation for the characteristic combination of gastrointestinal, neurological, and cardiovascular manifestations. Siegle and Pietsch (2024) used HPLC-MS/MS to demonstrate pronounced differences in alkaloid concentration between *Veratrum* species and plant organs, with some samples containing markedly higher levels than others. Such variability makes historical crude dosing especially hazardous because the same nominal mass of plant material may contain substantially different amounts of active alkaloids.

Contemporary human evidence is dominated by accidental intoxication rather than therapeutic trials. Rauber-Lüthy et al. (2010) described children who ingested *V. album* after plant collection for herbal tea; gastrointestinal and neurological symptoms were common and bradycardia occurred in several cases. Management is supportive, including cardiovascular monitoring, fluid therapy, correction of complications, and atropine when clinically important bradycardia is present; no specific antidote exists. Because potent cardiovascular effects can occur unpredictably and safer therapies are available, the modern significance of *Veratrum* lies mainly in pharmacognosy, ion-channel pharmacology, analytical toxicology, and poisoning prevention rather than in revival of crude internal therapy.

***Ricinus communis* L. - Castor Oil Plant**

Ricinus communis provides one of the clearest examples of why the medicinal value of a plant must be linked to a defined plant part and processing method. The seeds contain a high proportion of fixed oil together with the highly toxic protein ricin and the alkaloid ricinine. Chevallier, Duke, and PDR all distinguish between the toxic seed and properly prepared castor oil (Chevallier, 2016; Duke et al., 2002; Gruenwald et al., 2007). Castor oil has been used for centuries as a stimulant laxative, whereas ingestion of whole or chewed seeds may expose the patient to ricin and other seed constituents.

The major pharmacologically active component of castor oil is ricinoleic acid, released from triglycerides after intestinal hydrolysis. Experimental work has shown that ricinoleic acid activates prostaglandin EP3 receptors, providing a molecular basis for increased intestinal smooth-muscle activity and laxation. The same pathway also helps explain uterine contractile effects that have generated historical interest in castor oil during pregnancy; however, such use requires clinical supervision and should not be inferred from its laxative indication.

Ricin has a completely different mechanism. It is a ribosome-inactivating protein whose A-chain acts as an RNA N-glycosidase and removes a critical adenine from 28S ribosomal RNA, thereby disrupting protein synthesis (Endo & Tsurugi, 1987). Significant exposure can cause severe gastrointestinal illness and systemic organ injury; there is no specific routine antidote, and treatment is supportive (CDC, 2026). The pharmacognostic lesson is therefore fundamental: the statement that *R. communis* is medicinal is scientifically incomplete unless the preparation is specified. Pharmaceutical castor oil and ricin-containing seed material are chemically, pharmacologically, and toxicologically distinct products.

***Rauvolfia serpentina* (L.) Benth. ex Kurz - Indian Snakeroot**

Rauvolfia serpentina is an evergreen shrub of the Apocynaceae whose medicinal raw material is the root. It has a long history in South Asian medicine for insomnia, agitation, mental disorders, hypertension, and other conditions. Chevallier describes the root as a source of a complex mixture of indole alkaloids, including reserpine, rescinnamine, ajmaline, and related compounds; Duke similarly records hypotensive, sedative, and sympatholytic actions but emphasizes adverse effects and drug interactions (Chevallier, 2016; Duke et al., 2002). Georgian medicinal-plant literature also cites reserpine among important plant-derived pharmacologically active alkaloids (Bidzinashvili & Eradze, 2021).

Reserpine became one of the historically most important natural-product antihypertensive agents. Its principal mechanism involves inhibition of vesicular monoamine storage, which progressively depletes norepinephrine, dopamine, and serotonin from presynaptic terminals. Peripheral catecholamine depletion reduces sympathetic vascular tone and contributes to lowering of blood pressure, whereas central monoamine depletion helps explain sedation and some neuropsychiatric adverse effects. Ajmaline, another *Rauvolfia* alkaloid, acquired separate pharmacological importance as an antiarrhythmic compound. The species therefore illustrates how ethnomedical observations can direct research toward several chemically defined agents with distinct targets.

Human evidence for reserpine is stronger than for most crude poisonous plants reviewed here. A Cochrane review of randomized trials concluded that reserpine lowers systolic blood pressure compared with placebo, although the evidence base is relatively old and limited in size (Shamon & Perez, 2016). Its contemporary role has declined because alternative antihypertensive drugs are easier to titrate and because adverse effects may include hypotension, bradycardia, nasal congestion, gastrointestinal hypermotility, sedation, sexual dysfunction, and neuropsychiatric symptoms. Crude *Rauvolfia* root introduces additional uncertainty because it contains multiple alkaloids rather than a single controlled dose of reserpine. Thus, the scientific legacy of the plant lies principally in the pharmacology of isolated indole alkaloids and in the historical transition from ethnomedicine to modern cardiovascular and neuropharmacology.

Physostigma venenosum Balf. - Calabar Bean

Physostigma venenosum, the Calabar bean, is historically associated with both severe poisoning and the development of cholinergic pharmacology. The seeds contain physostigmine (eserine), a carbamate alkaloid with potent anticholinesterase activity. Duke and PDR emphasize that the seed itself is poisonous, while the isolated alkaloid has been of major pharmacological and clinical importance (Duke et al., 2002; Gruenwald et al., 2007). Georgian pharmacognostic literature likewise identifies physostigmine among important medicinal substances of plant origin (Bidzinashvili & Eradze, 2021).

Physostigmine reversibly inhibits acetylcholinesterase, increasing the persistence of acetylcholine at muscarinic and nicotinic synapses. Because it crosses the blood-brain barrier, its effects occur in both the central and peripheral nervous systems. Historically, this mechanism supported ophthalmological use, but its most distinctive contemporary role is in clinical toxicology, where physostigmine can reverse carefully selected cases of antimuscarinic delirium. Burns et al. (2000) reported substantially better control of delirium and agitation with physostigmine than with benzodiazepines in a comparative poisoned-patient cohort, illustrating the continuing medical relevance of a compound originally isolated from a highly toxic seed.

The same mechanism creates its own toxicity. Excessive cholinesterase inhibition may produce salivation, sweating, bronchial secretions, bradycardia, abdominal cramping, diarrhea, muscle fasciculations, weakness, and seizures. Physostigmine therefore requires professional patient selection and monitoring, particularly when mixed overdose or conduction abnormalities are suspected. This species represents a particularly instructive pharmacological paradox: an alkaloid derived from a poisonous plant is used as an antidotal medicine against toxicity caused by an opposing antimuscarinic mechanism. The success of physostigmine does not validate medicinal ingestion of Calabar bean; it validates isolation, chemical definition, dose control, and mechanism-based clinical use.

Podophyllum peltatum L. - American Mayapple

Podophyllum peltatum is a North American perennial whose rhizome and resin contain cytotoxic lignans, most notably podophyllotoxin. Historical uses included strong cathartic and emetic preparations and topical application to cutaneous lesions. Modern herbal references regard internal use of the crude plant as unacceptable because of substantial toxicity, while acknowledging the pharmaceutical importance of purified podophyllotoxin-related compounds (Chevallier, 2016; Duke et al., 2002; Gruenwald et al., 2007).

Podophyllotoxin inhibits tubulin polymerization and disrupts microtubule function, accounting for its antimitotic action. Its medical importance extends beyond the parent natural product because chemical modification of the podophyllotoxin scaffold yielded epipodophyllotoxin derivatives such as etoposide. Importantly, etoposide is not simply podophyllotoxin in another formulation: structural modification shifted the dominant mechanism toward topoisomerase II-mediated DNA

damage. This is a classic example of medicinal chemistry transforming a toxic natural-product scaffold into clinically valuable antineoplastic agents.

A separate therapeutic pathway concerns standardized topical podofilox/podophyllotoxin for external genital warts. Randomized controlled evidence demonstrated significantly greater wart clearance with patient-applied podofilox than with placebo, although local irritation and recurrence were common (Beutner et al., 1989). These data support a defined topical pharmaceutical concentration, not arbitrary use of crude podophyllin resin. Systemic absorption of resin may cause severe gastrointestinal symptoms, bone-marrow suppression, hepatic injury, neurological toxicity, and delayed peripheral neuropathy. No specific antidote exists. Podophyllum therefore illustrates perhaps the clearest progression from a hazardous botanical material to a purified topical agent and to semisynthetic systemic drugs with substantially altered pharmacology.

Rhododendron ponticum L. - Pontian Rhododendron

Rhododendron ponticum is of particular regional relevance because it is part of the relict vegetation of Georgia and the broader Colchic region. Kvachakidze identifies *R. ponticum* among Tertiary-relict elements and describes rhododendron-containing forest communities in western Georgia (Kvachakidze, 2009). Historical and folk uses of *Rhododendron* preparations or so-called "mad honey" have included pain, rheumatic complaints, gastrointestinal disorders, and cardiovascular purposes, but PDR and Duke treat the plant with considerable caution and do not support ordinary internal medicinal use (Gruenwald et al., 2007; Duke et al., 2002).

The principal toxicologically important constituents are grayanane diterpenoids, particularly grayanotoxins. These compounds interact with voltage-gated sodium channels and impair normal inactivation, promoting persistent depolarization. The resulting autonomic and cardiac effects may include nausea, vomiting, dizziness, sweating, bradycardia, hypotension, and atrioventricular conduction disturbances. Grayanotoxins may also be transferred to honey produced from *Rhododendron* nectar. Kurtoglu et al. (2014) demonstrated measurable grayanotoxins in mad honey and showed variation between samples, reinforcing the problem of unpredictable exposure.

Human literature is dominated by poisoning rather than therapeutic efficacy. Clinical series of mad-honey intoxication consistently describe marked bradycardia and hypotension, usually responding to monitoring, intravenous fluids, and atropine when clinically indicated. There is no specific grayanotoxin antidote. The fact that a toxic exposure can reduce blood pressure must not be interpreted as evidence for an antihypertensive treatment. For Georgia, *R. ponticum* is scientifically valuable for ethnobotanical documentation, phytochemical mapping, food-safety surveillance, and toxicological research, but its regional abundance does not justify therapeutic recommendation. This distinction is consistent with the broader Georgian ethnopharmacological principle that local knowledge should be preserved while subjected to modern pharmacognostic and clinical evaluation.

Table 1. Comparative pharmacognostic, pharmacological, and toxicological profile of the selected plants

Plant	Principal constituents / mechanism	Modern relevance	Major toxicological risk	Interpretation
H. niger	Hyoscyamine, scopolamine; muscarinic antagonism	Purified scopolamine; tropane-alkaloid research	Antimuscarinic delirium, tachycardia, hyperthermia, seizures	Value retained mainly through isolated alkaloids
V. album / V. lobelianum	Steroidal alkaloids; abnormal voltage-gated Na ⁺ channel activity	Analytical and experimental pharmacology	Vomiting, paresthesia, bradycardia, hypotension, arrhythmia	Predominantly toxicological; crude therapy not justified
R. communis	Ricinoleic acid (EP3 activation); ricin (ribosome inactivation)	Castor oil as stimulant laxative	Ricin-containing seed exposure may cause severe systemic poisoning	Preparation and processing determine whether product is medicinal or toxic
R. serpentina	Reserpine and related indole alkaloids; monoamine depletion	Historical antihypertensive; isolated alkaloids	Hypotension, bradycardia, sedation, neuropsychiatric effects	Ethnomedicine led to pharmacologically defined drugs
P. venenosum	Physostigmine; reversible acetylcholinesterase inhibition	Selected antidotal treatment for antimuscarinic delirium	Cholinergic excess, bradycardia, secretions, seizures	Poisonous seed yielded a controlled antidotal medicine
P. peltatum	Podophyllotoxin; tubulin inhibition; scaffold for etoposide	Topical podofilox and semisynthetic antineoplastic derivatives	Cytotoxicity, marrow and neurological injury after systemic exposure	Strong example of pharmaceutical transformation
R. ponticum	Grayanotoxins; impaired Na ⁺ channel inactivation	Food-safety, toxicology, analytical research	Bradycardia, hypotension, AV block	Regional relevance is high; therapeutic evidence is weak

Comparative Interpretation and Research Perspective

Comparative analysis reveals four broad translational models. First, in *H. niger* and *P. venenosum*, contemporary value is associated mainly with specific alkaloids whose pharmacology is sufficiently defined for controlled pharmaceutical use. Second, *P. peltatum* demonstrates the medicinal-chemistry model, in which a toxic natural compound became both a standardized topical agent and the structural origin of semisynthetic antineoplastic drugs. Third, *R. communis* demonstrates a processing model: a medicinal oil and a highly toxic protein occur in the same botanical source but must be treated as distinct products. Fourth, *V. album* and *R. ponticum* show that

demonstrable biological activity, including hypotension or autonomic effects, does not by itself establish a favorable therapeutic index. *R. serpentina* occupies an intermediate position because a historically used root directly stimulated the development of defined indole-alkaloid pharmacology, yet crude root preparations remain less predictable than purified drugs.

Across all seven species, standardization is the recurring scientific requirement. The plant name alone is insufficient. Pharmacognostic evaluation must specify the authenticated species, plant organ, stage of collection, drying and processing conditions, extraction procedure, chemical profile, and concentration of pharmacologically relevant constituents. This is especially important when the active substance has a narrow margin between therapeutic and toxic effects. The analytical variability documented for tropane alkaloids in *H. niger*, steroidal alkaloids in *Veratrum*, and grayanotoxins in *Rhododendron* illustrates why a historical "dose" of crude plant material cannot be assumed to produce a reproducible modern exposure (Ahmadpour et al., 2024; Siegle & Pietsch, 2024; Kurtoglu et al., 2014).

The Georgian context creates a valuable opportunity for integrated research. Historical and ethnobotanical records can guide selection of candidate species, while geobotanical data can establish regional occurrence and ecological context. These sources should then be linked to authenticated herbarium specimens, quantitative chromatographic profiles, toxicological metadata, and graded evidence fields that clearly separate traditional use, preclinical activity, human therapeutic evidence, and poisoning reports. This framework would preserve Georgian medicinal knowledge while avoiding the common error of treating historical use, pharmacological activity, and clinical efficacy as interchangeable concepts. The recent Georgian publications included in this review demonstrate the growing feasibility of such an interdisciplinary approach

A limitation of the present study is its narrative design. It was intended to synthesize pharmacognostic, historical, clinical, and toxicological perspectives rather than to perform a formal systematic review or meta-analysis. The evidence base is also heterogeneous: for some plant-derived products, such as podofilox and reserpine, controlled human studies exist, whereas for *Veratrum* and *Rhododendron* the most informative modern human literature consists largely of poisoning reports. This heterogeneity is itself an important finding because it shows that toxic medicinal plants should not be discussed as a single therapeutic category. Future work should prioritize species-specific authentication, quantitative phytochemistry, reproducibility of active-constituent content, pharmacokinetic characterization, and modern clinical evaluation only where a plausible therapeutic window exists.

Conclusions

The analysis of seven toxic medicinal plants confirms that toxicity and therapeutic potential are not mutually exclusive, but neither are they equivalent. A poisonous plant may contain molecules of major pharmacological value, yet historical use of the crude material cannot substitute for botanical authentication, chemical characterization, standardization, controlled dosing, clinical evaluation, and toxicological surveillance.

Hyoscyamus niger illustrates the transition from a dangerous anticholinergic herb to defined tropane-alkaloid pharmacology; *Veratrum album* demonstrates how potent sodium-channel-active alkaloids can make a historically used plant predominantly a toxicological subject; *Ricinus communis* shows that medicinal castor oil must be rigorously distinguished from ricin-containing seed exposure; *Rauvolfia serpentina* represents the historically important conversion of ethnomedical observations into reserpine and related indole-alkaloid pharmacology; *Physostigma venenosum* yielded physostigmine, a toxic natural alkaloid that became a clinically useful antidotal medicine; *Podophyllum peltatum* demonstrates both standardized topical use and successful semisynthetic drug development; and *Rhododendron ponticum* combines high Georgian phytogeographical relevance with a risk profile dominated by grayanotoxin poisoning.

The most scientifically defensible interpretation of poisonous medicinal plants is therefore not to seek a crude “therapeutic dose” for every historically used species, but to determine whether a reproducible and clinically useful biological signal can be transformed into a standardized intervention whose benefit exceeds risk. For Georgian ethnopharmacology, the integration of historical knowledge, local flora, authenticated botanical material, modern phytochemical analysis, and explicit evidence grading offers a productive path for future research while preserving both scientific rigor and patient safety.

References

1. Ahmadpour, R., Maleki Zanjani, B., Garoosi, G.-A., Farjaminezhad, R., & Haddad, R. (2024). Ultrasound-assisted extraction of scopolamine and hyoscyamine from *Hyoscyamus niger* roots using central composite design. *Heliyon*, 10(19), e38856. doi:10.1016/j.heliyon.2024.e38856
2. Beutner, K. R., Conant, M. A., Friedman-Kien, A. E., Illeman, M., Artman, N. N., Thisted, R. A., & King, D. H. (1989). Patient-applied podofilox for treatment of genital warts. *The Lancet*, 1(8642), 831-834. doi:10.1016/S0140-6736(89)92282-4
3. Bidzinashvili, R., & Eradze, N. (2021). *Samkurnalo mcenareebis kultura: Salekcio kursi* [Medicinal plant cultivation: Lecture course]. Mtsignobari.
4. Burns, M. J., Linden, C. H., Graudins, A., Brown, R. M., & Fletcher, K. E. (2000). A comparison of physostigmine and benzodiazepines for the treatment of anticholinergic poisoning. *Annals of Emergency Medicine*, 35(4), 374-381. doi:10.1016/S0196-0644(00)70057-6
5. Centers for Disease Control and Prevention. (2026). Ricin: Chemical emergency fact sheet.
6. Chevallier, A. (2016). *Encyclopedia of Herbal Medicine: 550 Herbs and Remedies for Common Ailments* (3rd ed.). DK Publishing.
7. Duke, J. A., Bogenschutz-Godwin, M. J., duCellier, J., & Duke, P.-A. K. (2002). *Handbook of Medicinal Herbs* (2nd ed.). CRC Press.
8. Endo, Y., & Tsurugi, K. (1987). RNA N-glycosidase activity of ricin A-chain: Mechanism of action of the toxic lectin ricin on eukaryotic ribosomes. *Journal of Biological Chemistry*, 262(17), 8128-8130.

9. Gruenwald, J., Brendler, T., & Jaenicke, C. (Eds.). (2007). PDR for Herbal Medicines (4th ed.). Thomson Healthcare.
10. Kochadze, D., Latchkepani, E., & Makharashvili, R. (2025). Traditional Georgian ethnopharmacology: Historical foundations, medicinal plant cultivation practices, and knowledge transmission pathways. *Georgian Scientists*, 7(2), 730-744. doi:10.52340/g.s.2025.07.02.69
11. Kochadze, D., Latchkepani, E., Makharashvili, R., Dolidze, N., & Asanidze, N. (2025a). Medicinal geophytes as natural antimicrobial agents - An ethnobotanical review on the example of Georgia. *Georgian Scientists*, 7(3), 454-467. doi: 10.52340/g.s.2025.07.03.27
12. Kochadze, D., Latchkepani, E., Makharashvili, R., Mgaloblishvili, N., Kuchukhidze, D., Chkhaidze, B., ... Asanidze, N. (2025b). The history of the development of herbalism: From shamanism to scientific medicine. *Georgian Scientists*, 7(4), 311-325. doi:10.52340/g.s.2025.07.04.16
13. Kochadze, D., Latchkepani, E., Makharashvili, R., & Silagadze, N. (2026). Pharmacognostic profile and ethnopharmacological significance of selected medicinal plants growing on Mount Khvamli. *Health Policy, Economics and Sociology*, 10(2). <https://doi.org/10.52340/healthecosoc.2026.10.02.3>
14. Kurtoglu, A. B., Yavuz, R., & Evrendilek, G. A. (2014). Characterisation and fate of grayanotoxins in mad honey produced from *Rhododendron ponticum* nectar. *Food Chemistry*, 161, 47-52. doi: 10.1016/j.foodchem.2014.03.127
15. Kvachakidze, R. (2009). *Sakartvelos mcenareuloba* [Vegetation of Georgia]. Tbilisi Botanical Garden and Institute of Botany.
16. Melikishvili, G. (Ed.). (1970). *Sakartvelos istoriis narkvevebi* [Essays on the History of Georgia] (Vol. 1). Sabchota Sakartvelo.
17. Rauber-Lüthy, C., Halbsguth, U., Kupferschmidt, H., König, N., Mégevand, C., Zihlmann, K., & Ceschi, A. (2010). Low-dose exposure to *Veratrum album* in children causes mild effects - A case series. *Clinical Toxicology*, 48(3), 234-237. doi:10.3109/15563650903575243
18. Shamon, S. D., & Perez, M. I. (2016). Blood pressure-lowering efficacy of reserpine for primary hypertension. *Cochrane Database of Systematic Reviews*.
19. Siegle, J., & Pietsch, J. (2024). Determination of *Veratrum* alkaloid contents in three *Veratrum* species by HPLC-MS/MS. *Phytochemical Analysis*, 35(7), 1577-1586. doi:10.1002/pca.3401
20. Terzi, K., Ersan, F. G., & Sarıtaş Nakip, Ö. (2026). The toxicity of *Hyoscyamus niger* (henbane) in children: A five-year experience in a pediatric intensive care unit. *Clinical Toxicology*. Advance online publication. doi:10.1080/15563650.2026.2655383