Published in final edited form as:

Clin Toxicol (Phila). 2018 September ; 56(9): 841–845. doi:10.1080/15563650.2018.1442007.

Hikers poisoned: *Veratrum* steroidal alkaloid toxicity following ingestion of foraged *Veratrum parviflorum*

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Abstract

Introduction—Steroidal alkaloids are found in plants of the genus *Veratrum*. Their toxicity manifests as gastrointestinal symptoms followed by a Bezold–Jarisch reflex: hypopnea, hypotension, and bradycardia. Some *Veratrum* steroidal alkaloids are also teratogens interfering with the hedgehog-2 signaling pathway, which causes cyclopsia and holoprosencephaly. We present a case of accidental poisoning from *Veratrum parviflorum* mistaken for the edible *Allium tricoccum* (ramps, wild leek).

Case history—A 27-year-old man and his 25-year-old wife presented to the emergency department with nausea, vomiting, hypotension, and bradycardia after foraging and ingesting plants that they believed to be a local native species of wild leek.

Methods—We collected and analyzed the implicated fresh plant material and both patients' serum/plasma. We used liquid chromatography–mass spectroscopy and high-resolution electrospray ionization time of flight tandem mass spectrometry to extract and characterize steroidal alkaloids from the foraged plant and patients' serum.

Results—Our *V. parviflorum* samples contained verazine, veratramine, veratridine, and cyclopamine.

Discussion—Steroidal alkaloids have been previously isolated from *Veratrum viride* and *Veratrum album* and toxicity has been reported mainly from *V. album* species.

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Supplemental data for this article can be accessed [here](#).

Disclosure statement

No potential conflict of interest was reported by the authors.

Conclusion—*V. parviflorum* toxicity manifests with gastrointestinal and cardiac symptoms. Treatment is symptomatic and supportive as with previous case reports of toxicity with other *Veratrum* species.

Keywords

Steroidal alkaloid; *Veratrum*; wild leeks; cyclopamine; Bezold–Jarisch

Introduction

The nine species (or species complexes) of the plant genus *Veratrum* found in North America include: *Veratrum album*, *Veratrum californicum*, *Veratrum parviflorum*, *Veratrum tenuipetalum*, and *Veratrum viride* [1,2]. They are generally referred to as false hellebores or bunchflowers [3]. *V. parviflorum* (mountain bunchflower; synonym: *Melanthium parviflorum*) is restricted to forested mountain slopes (at least 1700 m) in the southeastern USA [4]. Mature plants with flowering stalks are approximately 1–2 +m tall, with a short rhizome plus a small bulb, and a pseudostem formed by the overlapping sheaths of the broad, oval to elliptical leaves [2,5] (Figure 1).

Veratrum species can contain many steroidal alkaloids, including the veratrinine (veratridine, veratrine, etc.), jervanine (cyclopamine, cycloposine, jervine, etc.), cevanine, verazine, and solanidine types [3,6]. *Veratrum* steroidal alkaloids such as veratramine and veratridine cause neuronal sodium channel hyperpermeability, leading to toxicity that manifests initially with gastrointestinal symptoms followed by a Bezold–Jarisch reflex of hypopnea, hypotension, and bradycardia [7]. The cardiogenic effects of *Veratrum* alkaloids were investigated for therapeutic use in hypertension but this work was abandoned due to its narrow therapeutic index [3]. *Veratrum* steroidal alkaloids of the jervanine type, such as cyclopamine, are teratogens interfering with the hedgehog-2 signaling pathway, which causes cyclopsia and holoprosencephaly. This pathology was originally described in ewes whose pregnant mothers grazed on *V. californicum* [8]. Human teratogenicity has not been reported. More recently, cyclopamine and cyclopamine derivatives have been investigated as potential therapeutics in cancer [9].

Reports of acute *Veratrum* toxicity in the literature are mainly from *V. album* and *V. viride*. Toxicity has occurred when *Veratrum* species were mistakenly identified as wild leeks or ramps (species of *Allium*), whose leaves and bulbs superficially resemble those of *Veratrum* in the vegetative (non-flowering) state. Treatment is supportive and symptomatic care with severe cases requiring hemodynamic support with atropine, intravenous fluids, or vasopressors. Resolution of symptoms usually occurs within 24 h but can persist longer. A few cases of severe toxicity requiring cardiopulmonary resuscitation and resulting in death have been described [10–13]. Because the primary cardiotoxic manifestation of its poisoning resembles cardiac glycoside toxicity, digoxin immune Fab has been used as empiric treatment, but has not been shown to bind *Veratrum* alkaloids [14].

Case history

A 27-year-old man (patient 1) and his 25-year-old wife (patient 2) presented to a community emergency department in April 2015 with nausea and vomiting after foraging and ingesting plants (Figure 2) that they believed to be a local native species of wild leek (Figure 3, *Allium tricoccum*) collected along the Appalachian Trail in Union County, Georgia, USA. Patient 1 had a blood pressure of 87/40 mmHg and a heart rate of 53 beats per minute, and patient 2 had a blood pressure of 88/40 mmHg and a heart rate of 50 beats per minute. They received antiemetics and fluid resuscitation. They were alert and awake, and electrocardiograms showed sinus bradycardia. Ten vials of digoxin immune Fab were given due to concern for possible cardiac glycoside toxicity. The local poison center was consulted after initial treatment. No further treatments were recommended, as patients were no longer symptomatic. Laboratory analysis showed undetectable digoxin levels in both patients. Their symptoms resolved 12 h after arrival, and they were discharged within 34 h. The plant was identified from leaf material by University of Georgia botanists as *V. parviflorum* two week(s) later.

Materials and methods

Voucher deposition

Some leaves and attached stem were prepared as a pressed specimen voucher and deposited in the University of Georgia Herbarium collection (specimen bar-code number: GA221668).

The uneaten cooked plant specimen was prepared for chemical analysis by lyophilization and extraction. The extract was purified by solid phase extraction (SPE) for chemical characterization. Chromatographic separation of samples was carried out using a Dionex Ultimate 3000 HPLC system. Analysis of samples was performed using high resolution Bruker Daltonics maXis Quadrupole Time-of-Flight (Q-TOF) mass spectrometer operated with an electrospray ionization (ESI) source. All samples were subjected to LC–MS analysis, and extracted ion chromatograms (EIC) were generated and used to characterize the constituents (see online supplemental file for further details on biomass component extraction, sample preparation, and LC–MS analysis).

Results

Four alkaloids previously isolated from *Veratrum* species were identified from the extracted biomass of *V. parviflorum*: verazine (m/z 398.3125), veratramine (m/z 410.3141), cyclopamine (m/z 412.3285), and veratridine (m/z 674.4174). The analyzed biomass had been cooked in water: the heating process did not destroy the isolated alkaloids and the alkaloids were still present in the plant material. In summary, the ions with identical m/z and retention times observed in the extracted biomass and patient samples constituted 23.64% (13 of 55), 14.55% (8 of 55), and 25.45% (14 of 55) for Patient 1 plasma, Patient 1 serum, and Patient 2 plasma, respectively (see online supplemental file for detailed results and figures on mass spectrometry data).

Discussion

Steroidal alkaloids have been previously isolated from many species of *Veratrum* and toxicity has been reported mainly from *V. album* and *V. viride* [3,6]. Our *V. parviflorum* samples contained verazine, veratramine, veratridine, and cyclopamine. The alkaloids differ from those of *V. album* that has proverafrine A, proverafrine B, jervine, cevadine, as well as veratridine [15,16], and *V. viride*, which contains veramarine, angeloylzygadenine, zygadenine, 15-O-methylbutyroylgermine, 1a,3sz-dihydroxy-5a-jervanin-12-en-11-one, veratramine, jervine, isorubijervine, germine, rubijervine, and pseudojervine [17]. The symptoms displayed by the patients in our case, which included nausea, vomiting, hypotension, and bradycardia, are consistent with those reported for *Veratrum* toxicity. The latency and duration of action are also within prior reported limits. However, neurological symptoms, such as taste disturbance, vertigo, dysarthria, and vision changes, were not reported with cases of toxicity with *V. album* and *V. viride* [13,18]. The difference in toxicity may be related to the mixture of alkaloids found in each respective species, the particular plant parts consumed, time of year the plant was collected, geographical location, and cooking method. The variability in alkaloid composition and/or concentration depending on stage of development or time of year is not currently known, although all parts of the plant are reportedly toxic [3]. Also, the duration of time between collection and sample analysis may affect toxicity, and some alkaloids may have undergone degradation by the time of our analysis two weeks after ingestion.

The clinician in a community emergency department setting provided appropriate symptomatic and supportive treatments such as ondansetron and intravenous normal saline. Digoxin immune Fab was given prior to poison center consultation. This may have been done for undifferentiated cardiotoxicity after plant ingestion. In one case, steroidal alkaloids were shown to cross-react with the laboratory Digoxin immunoassay, but Digoxin immune Fab was not given in that case as the treating clinician was able to identify the plant as *V. viride* [14].

Conclusion

V. parviflorum contains the *Veratrum* alkaloids verazine, veratramine, veratridine, and cyclopamine. Its acute toxicity manifests with gastrointestinal and cardiac symptoms. Treatment is symptomatic and supportive as with previous case reports of toxicity with other *Veratrum* species.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

We thank Dr. David E. Giannasi, University of Georgia Herbarium, for assisting WBZ in confirming the plant identification.

Funding

Support for graduate student Matthew W. Turner and seed funding for HPLC and MS for the project described was supported by Institutional Development Awards (IDeA) from the National Institute of General Medical Sciences of the National Institutes of Health under Grants [#P20GM103408] (INBRE) and [P20GM109095] (COBRE in Matrix Biology). We also acknowledge support from the Biomolecular Research Center at Boise State with funding from the National Science Foundation [Grants # 0619793 and #0923535]; the MJ Murdock Charitable Trust; and the Idaho State Board of Education. Contents are solely the responsibility of the authors and do not necessarily represent the official views of NIH.

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Figure 1.
Herbarium specimen of a mature plant of *Veratrum parviflorum* collected in Lumpkin County, Georgia (University of Georgia Herbarium barcode GA021971).

Figure 2.
Live sample of a plant foraged by the patients. The bulb was removed for consumption.

Figure 3. Herbarium specimen of *Allium tricoccum* (ramps, wild leek) collected in Union County, Georgia, in the spring before flowering (University of Georgia Herbarium barcode GA022180). The leaves and edible bulb of this species superficially resemble those of the poisonous *Veratrum parviflorum*.