Hemlock poisoning due to plant misidentification

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Abstract

A case report (two patients) of accidental intoxication occurred in Northern Italy. *Conium maculatum* L. (poison hemlock) leaves were confused with and collected as *Foeniculum vulgare* Mill. (sweet fennel). *C. maculatum* contains piperidine alkaloids: coniine, N-methylconiine, conhydrine, pseudoconhydrine and □-coniceine, toxic to human beings. Identification and microscopic examination of the consumed plants were according to clinical signs of patients. Haematological and biochemical indices in blood, morphological alterations and the effect of the treatment were directly related to the intoxication. The patients were discharged alive and well after 3 days of supportive treatment.

Keywords: Accidental intoxication, coniine analysis, *Conium maculatum*

Introduction

Plant self-collection is dangerous when performed without knowledge in plant morphology. In this note we report a severe toxic reaction to hemlock mistakenly gathered as wild fennel. Fennel is widely distributed in Mediterranean areas, it is used as spice and medicinal plant [www.ars-grin.gov].

The toxicity of hemlock is due to piperidine alkaloids: (+)-coniine, N-methylconiine, (+)-conhydrine, pseudoconhydrine and γ-coniceine (Figure 1). γ-Coniceine and coniine are the most abundant alkaloids, present also in tropical plants such as Aloe species [1].

Coniine a pale yellow, oily alkaloid, volatile at r. t.; is a neurotoxin for humans, causing death by respiratory paralysis, the most famous was Socrates in 399 BC [2]. Hemlock poisoning also causes rhabdomyolysis and acute renal failure [3], dermatitis can result from merely handling the plant [www.intox].

Case report. A man and his wife were admitted one hour after they had had dinner to the Emergency Department of Brescia Hospital with nausea, painful leg cramps, dilated and unresponsive pupils and dizziness. The symptoms were associated with the consumption of wild plants. The patients had gathered from beside a ditch what they thought were *Foeniculum vulgare* Miller (sweet fennel), an aromatic herb [4]. For dinner the woman ate both fresh and boiled vegetables, while her husband ate only boiled. Within few minutes the woman complained nausea, dizziness, accomodation defects, painful leg cramps, neck and shoulders orticarioid rash. She was admitted to the Emergency Room and gastrolusis was performed. Then she was admitted to the Department of Anaesthesiology and Reanimation because she needed neurological and cardiovascular monitoring. She was treated with activated carbon and magnesium sulphate. Diuresis was forced by large volume fluid infusion : 7000 mL/24h (first day), 3000 mL (second day) and 1500 mL (third day). Neurological symptoms progressively regressed, after 48 hours she complained episodic leg trembling lasting only few minutes; nausea and leg paresthesias persisted for three days. During instrumental and clinical monitoring no cardiac arrhythmias were detected; renal function and total CPK enzymes were in the normal range at the admission and during the following days.

The man had milder symptoms: general discomfort and mild painful leg cramps at the admission in the Emergency Room. Renal function and total CPK enzymes were in the normal range. He was treated following the same protocol adopted for his wife in the Department of Anaesthesiology and Reanimation. After a

few hours he didn't complain any symptom.

Materials and Methods

Plant material

Fragments 8 – 10 cm long of the fresh stems of the harvested plants were photographed to record their natural coloration, and the piperidine alkaloids they contained were analysed.

Coniine standard solutions

Coniine (2-propylpiperidine) [Sigma-Aldrich Co., St. Louis, USA] purity ≥ 98%, light yellow liquid at r. t. , was dissolved in HCl 0.01N (0.85 mg/mL stock solution). Before use, the stock solution was further diluted in HCl 0.01N to 0.085 and 0.0085 mg/mL.

Alkaloid extraction from plant material

The plant material (2.00 g fresh weight) was ground in a mortar with 0.01 N HCl (1:10 w/v). After agitation for 1 h at r. t. , the solution was filtered and the residue was re-extracted with fresh 0.01 N HCl (1:10 w/v) in the same way. The combined acidic solutions were used for qualitative and quantitative analysis. Final volume was 20 mL per gram of extracted product.

Qualitative coniine analysis on plant material

The plant extract (4 mL), a coniine standard solution 0.85 mg/mL and a blank solution of HCl 0.01N were treated in parallel. The piperidine alkaloids were precipitated with an equal volume of saturated Reinecke's salt $NH_4[Cr(SCN)_4(NH_3)_2]$ in 0.5 M HCl. The reaction was performed in an acidic aqueous solution, and the reaction products of Reinecke's salt with the piperidine alkaloids were precipitated after incubation for 1 h at +4° C [5, 6]. The precipitated crystals were examined in a light microscope Axioskop Zeiss 40 FL, equipped with the digital microscope camera Zeiss Axiocam HR (Zeiss Italia, Arese, MI).

Qualitative coniine analysis on patients' urine

For alkaloid analysis, 0.5 mL of urine was added to 0.5 mL HCl 0,01N and 1 mL of a saturated solution of Reinecke's salt solution. After 10 min under vortex agitation, the reaction mixture was centrifuged for 10 min at 5000 rpm; the upper layer was removed, and the precipitate was suspended in 2 mL acetone. The precipitated crystals were observed in the light microscope as above.

Quantitative coniine analysis on plant material

The coniine standard solutions (0.85, 0.085 and 0.0085 mg/mL) and the plant extracts were neutralised with NaOH 1N. Then to 500 µL of each solution were added 1.5 mL of acetone, 2 mL of pirocatechin solution (0.5 ‰ in acetone) and 5 mg of Ag_2O crystals. The reaction mixtures, vortexed for 1 min and then incubated 3 h at r. t. , were read by spectrophotometry at 520 nm [7].

Quantitative coniine analysis in urine

The urine (1 mL) was neutralised with NaOH 1N, and 500 µL of the solution was examined as in the previous paragraph.

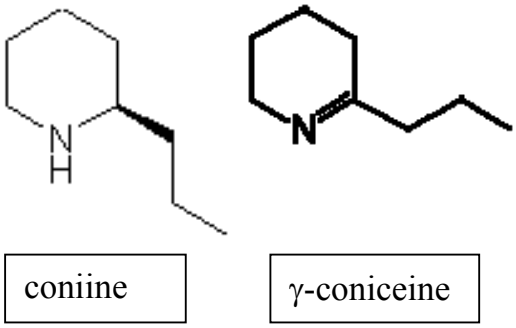


Figure 1: Chemical structure

Results and Discussion

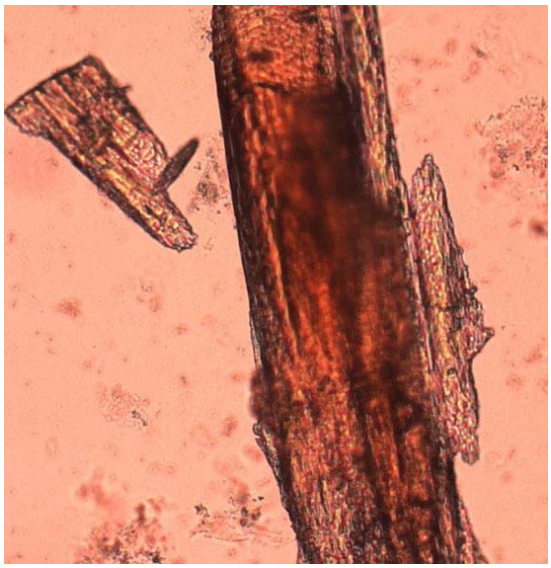
Botanical examinations

The macroscopical examination of the leaves and particularly of the stem led to the suspicion that the collected plants were *Conium maculatum* L. (poison hemlock). This is a species of Apiaceae (formerly Umbelliferae) family, characterised by long, hollow stems, reaching up to 2 m height at maturity, producing a large amount of lush foliage during its vegetative growth. Its flowers are white, grouped in umbels formed by numerous

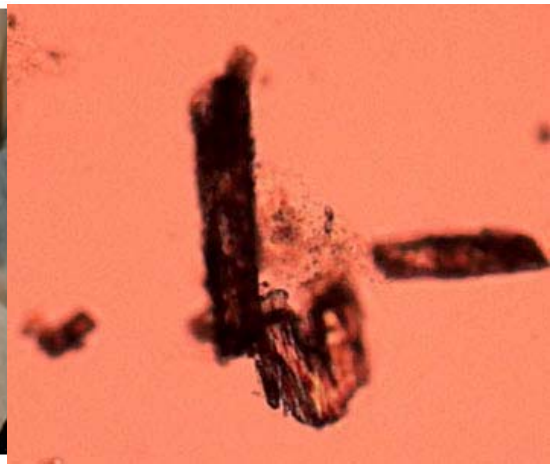
A

B

Figure 2



A



B

Figure 3

umbellules. It produces a large number of seeds that allow the plant to form thick stands in modified soils, sometimes encroaching on cultivated fields to such an extent that they impede the growth of other vegetable matter. The species name *maculatum*, spotted, refers to the characteristic brownish-reddish spots on the stem. *C. maculatum* is a weed widely known for its toxicity for many domestic animals and human beings.

The identification of the wild plant in this case as *Conium maculatum* L. was based on observation of the stems, which were typically glabrous, green, hollow except at the internodes (Figure 2 panel a and panel b) and with purple spots on the surface. When crushed, the stem had a nauseous 'mousy' smell. The stem epidermis was striated, with collenchymatous venation. On the basis of morphological and organoleptic observations, we could confirm the identification. The botanical identification was in agreement with the symptoms complained of by the patients, who after a supportive and symptomatic therapy for three days, were completely asymptomatic, and discharged.

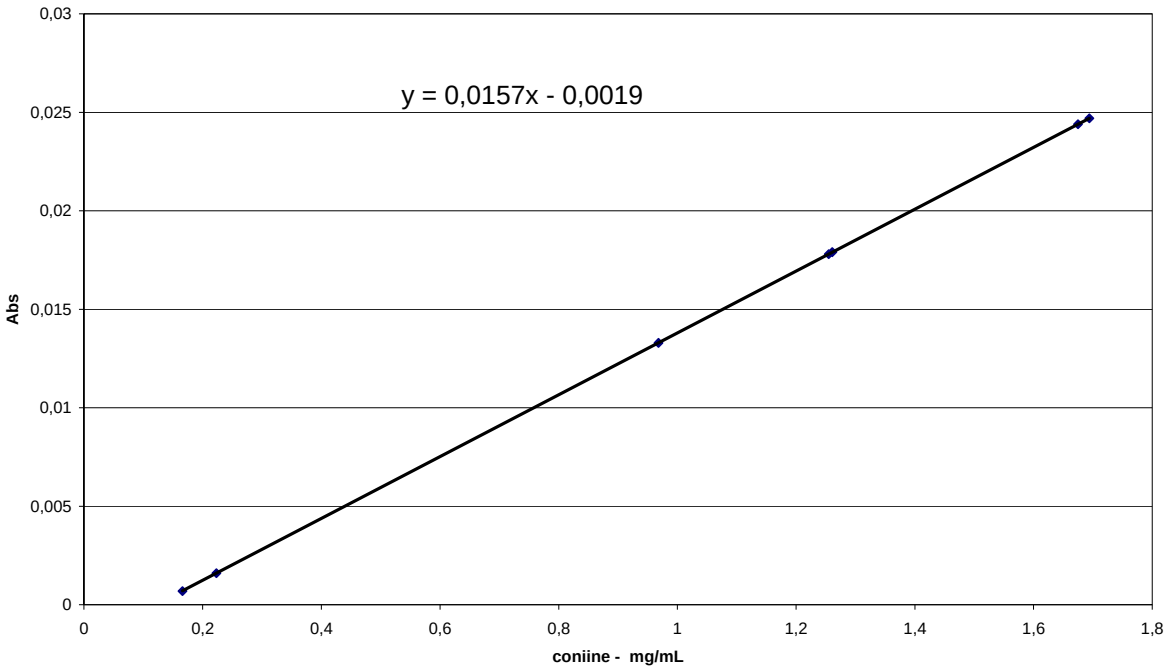


Figure 4

Qualitative analysis of alkaloids

Alkaloids are bases having the common characteristic of containing a heterocyclic nitrogen and are usually toxic. They are otherwise very different, in term of structure, volatility, stability, and polarity. Unlike other alkaloids, coniine (Figure 1) is volatile. In view of this property, in order to characterise the base we converted it into one of its non-volatile salts. Coniine chloride is very suitable for the purpose, as it crystallises in easily recognisable long, double-refracting, silky needles [5]. By using a selective precipitation reaction with Reinecke's salt, which is known to selectively trap quaternary ammonium alkaloids, we were able to detect coniine. The addition of Reinecke's salt (ammonium tetracyanato diamine chromate) permitted the secondary amine coniine to be precipitated as an insoluble salt [6]. Chromium is here in the 3^+ oxidation state, surrounded by six ligands in an octahedral geometry; the NH_3 ligands are mutually trans [5]. The crystals resulting from amine precipitation can be examined in micrographs in a preliminary qualitative analysis (Figure 3 panel a). Very similar results were obtained with the patients' urine (Figure 3 panel b).

Quantitative analysis of coniine alkaloid content

The analyses were performed using the chemical characteristics of coniine. It is soluble in alcohol, ether and acetone. With pyrocatechin and Ag_2O it yields a coloured derivative, which turns violet when acetone is present. The coniine content was calculated on the basis of the linear regression obtained with coniine standard solutions (Figure 4).

The *C. maculatum* stems obtained from Brescia Hospital contained coniine at 0.98 ± 0.03 g/100g d.w. The reported content accords with data in the literature [8] and was high enough to cause the toxic effects observed.

Conclusions

Misidentification of poison hemlock with other members of the same family is common and can be fatal. In the case described, the poison hemlock was mistaken for sweet fennel, an obvious mistake which should be easily avoided.

Sweet fennel and poison hemlock have different and very characteristic smells: aromatic, licorice-like flavour in sweet fennel, foetid and 'mousy' in poison hemlock. The leaves, stem and flowers of fennel and poison hemlock are very different in morphology.

Other misidentifications are possible: *Conium maculatum* roots can be easily confused with the edible root of wild parsnip (*Pastinaca sativa* L.), with deadly results. The 'seeds' (dry fruits, achenes) of poison hemlock are sometimes collected in mistake for anise fruits, *Pimpinella anisum* L. [8]. We have to remember that poisonous plants can have different adverse effects on animals; don't assume that since a caterpillar, bird, squirrel or pig ate a plant with no problems, others (human or rabbit) can do the same [8, 9]. Some examples are reported of the meat of birds having had dangerous, or even fatal effects, on men eating the birds, *e.g.* quail *Coturnix coturnix*, after eating the seeds of hemlock, *Conium maculatum* [10]. Such a toxicological syndrome (also called coturnism, human poisoning after eating contaminated quail) occurs during the migration of quails from North to South, when the birds consume hemlock seeds. The clinical symptoms of intoxicated people are indicative of acute rhabdomyolysis [11].

In conclusion, the ingestion of poison hemlock can lead to serious complications that may be fatal: prognosis is good if prompt supportive care is provided.

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