CASE REPORT

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Colchicine Poisoning as a Mode of Suicide

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ABSTRACT: Two cases of suicide involving colchicine are examined. Colchicine and colchicum preparations have been used for the relief of pain in acute gout and are reported to be effective for the treatment of periodic peritonitis. A method using enzymatic digestion, extraction, and high pressure liquid chromatographic analysis for the extraction and analysis of colchicine in autopsy specimens is described.

KEYWORDS: toxicology, colchicine, poisons

Colchicine is an alkaloid obtained from the corm and seeds of meadow saffron, *Colchicum* species (Liliaceae) [*1-3*]. Colchicine and colchicum preparations have been used for the relief of pain in acute gout [*3,4*] and are reported to be effective for the treatment of periodic peritonitis (as well as for recurrent polyserositis and familial Mediterranean fever) [*1*]. The total amount of colchicine required to relieve an acute attack of gout is between 3 to 6 mg. A total dose of 6 mg should not be exceeded during a single course of treatment, and a total dose of 3 mg should not be exceeded in 26 h [*3*].

When orally ingested, colchicine is rapidly absorbed from the gastrointestinal tract and passed on to the liver, where it is metabolized via deacetylation and demethylation. Large amounts of drug and metabolites are excreted in the bile and, via the blood, into the intestinal tract, resulting in an enterohepatic circulation [*4,5*]. This rapid circulation would probably account for the gastrointestinal side effects observed: severe abdominal pain, nausea, vomiting, and diarrhea characteristic of colchicine poisoning. Symptons of poisoning set in only after an interval of 3 to 6 h, even with large doses, resulting in a pronounced muscular depression and an ascending paralysis of the central nervous system (CNS), with death occurring from respiratory arrest generally within one to two days [*1,3,4*]. The lethal dose varies considerably; as little as 7 mg of colchicine has proved fatal while larger doses have been survived [*1,3*].

A number of techniques have been used to determine colchicine concentrations in biological fluids, namely colorimetry, [*6,7*], radioimmunoassay [*8*], and high pressure liquid

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chromatography (HPLC) techniques [*9,10*]. This paper describes a method using HPLC to determine colchicine in biological material.

Case Reports

Case 1

A 61-year-old single man was found dead beside his bed at 12:15 p.m. by a "Meals-on-Wheels" service worker. Beside the body was found a quantity of tablets and three bottles labelled "Serepax," "Prednisone," and "Colchicine"; the latter two bottles were empty. On a cupboard near the body was a glass mug containing an amber-colored liquid (beer) and a large quantity of white sediment. The deceased had been treated for scleroderma and had recently been released from the hospital.

Autopsy revealed massive edema and moderate congestion of the lungs. The bronchi, larynx, and trachea contained a copious amount of mucopurulent secretion. The trachea and bronchial mucosa were moderately congested. Examination of the gastrointestinal tract revealed the esophagus was thickened in its lower part and the mucosa appeared to be slightly sclerosed. The stomach contained approximately 400 mL of recently eaten food.

The stomach mucosa was slightly congested. Small and large intestines were normal. Liver, bile, and stomach specimens were collected for toxicological analysis.

Case 2

A 23-year-old single unemployed man swallowed 25 to 50 mg of colchicine in tablet form ("Colgout") with suicidal intent. As a result of this ingestion he became ill and contacted his mother by telephone to get an ambulance. His mother found him unconscious. A short time later he was conveyed to a hospital. Two days later, he apparently suffered a major cardiac arrest and died.

Autopsy revealed marked edema of the lungs. The respiratory passages contained some frothy bloodstained mucus. Examination of the gastrointestinal tract revealed marked paraesophageal hemorrhage. The stomach contained some bloodstained fluid, and a few small hemorrhages were present in the gastric mucosa. Hemorrhages were also present in the mucosa and wall of the small intestine in numerous places. Liver, urine, and stomach specimens were collected for toxicological analysis.

Method of Analysis

The reagents used to determine the colchicine concentrations are as follows:

(1) crystalline Subtilisin Carlsberg (Novo, Sweden) (also known as Protease Type VIII),

(2) tris(hydroxymethyl)aminomethane (Tris) buffer or base (Merck Chemicals, Darmstadt),

(3) chloroform, analytical reagent grade (Ajax Chemicals, Sydney),

(4) methanol, analytical reagent grade (Mallinckrodt Chemical Co., St. Louis, MO), and

(5) colchicine base (Sigma Chemical Co., St. Louis, MO).

The liquid chromatograph was a Waters Associates (Milford, MA) Model 440 equipped with a WISP 710A automatic injector and a variable wavelength ultraviolet (UV) detector (Model 450). The column was a 25-cm reverse-phase 10-μm "Bondapak" C-18 from Waters. The solvent system was 50:50 mixture of methanol and water. The flow rate was 1.5 mL/min, the chart speed was 0.5 cm/min, and the UV detector was set at 243 nm. A Waters Data Module integrating recorder was used for collection of data.

A standard solution was prepared from a methanolic stock solution containing 1.00

mg/mL of colchicine base. A final working solution of 0.01 mg/mL was used in subsequent analysis, 15- to 20-μL aliquots being injected.

Portions of liver (10 g) from each case were blended with Tris base (40 mL, 121 g/L, pH 10.5) in 100-mL conical flasks. Crystalline Subtilisin was added to the blended tissue samples (1 mg of enzyme per gram of liver) with gentle swirling prior to incubation at 55 to 60°C for 1 h with continuous shaking in a thermostated water bath (Grant Instruments, Cambridge) [*11*].

The homogenates (at final pH of 8.5 to 9) were cooled prior to extraction of the drug from the aqueous phase by shaking twice with 50 mL of redistilled chloroform. The chloroform extracts were combined and back-extracted into 20 mL of 1*M* sulfuric acid, which was in turn rendered alkaline (pH 9) with 2*M* sodium hydroxide, and re-extracted with chloroform. This step removed much of the colored endogenous material derived from the enzyme digest. The extracts were then evaporated under nitrogen. The dried extracts were diluted to 10 mL in a volumetric flask with methanol.

The biological fluids (5 mL), urine and bile, were transferred to a capped polyethylene centrifuge tube; to each tube was added 1 mL of 1*M* sodium phosphate buffer (pH 7.5) and then 5 mL of chloroform. The samples were placed on a rocking table for 15 min. The homogenate was then centrifuged at 1500 rpm for 10 min. A portion of the supernatant was drawn off with a glass syringe and evaporated under nitrogen. The dried extracts were reconstituted with 5.0 mL of methanol and subsequently injected into a HPLC.

Recovery Studies

Recovery studies were carried out using drug-free liver and urine samples; 300- and 150-μL aliquots from the methanolic colchicine standard (1.00 mg/mL) were added to liver homogenates (10 g) and urine samples (5 mL), respectively. The spiked samples were treated as above after standing at room temperature for 1 h.

Colchicine in the extract solutions was quantitated by comparing the peak areas of several injections to the peak area of a colchicine standard (0.01 mg/mL).

Results and Discussion

The results of initial chromatography and of toxicologic analysis are presented in Tables 1 and 2.

Recovery studies revealed the following: from enzymatic liver digestion an average of 95 to 97% was recovered, and 85% was recovered from pH 7.5 urine with the previously described single extraction procedure with chloroform. Evidently the proteolytic enzyme treatment was more effective in releasing the drug [*11*].

Toxicologic analysis of the thick white sediment in the glass mug (Case 1) revealed the presence of prednisone, colchicine, and the decomposition product lumicolchicine.

TABLE 1—*Chromatography data.*

Drug	R_f,[a] × 100	R_T,[b] min	λ_{max}[c] (Ethanol)	Log ϵ[d]
Colchicine	58	5.06	243.5, 351	4.21, 4.45
Colchiceine	30	6.56	243, 350.5	4.22, 4.47
Lumicolchicine	78–80	7.73	...	...

[a]Thin-layer chromatographic system: chloroform/acetone/diethylamine, 70:20:10.
[b]Retention time; HPLC system: methanol/water, 50:50; detector set at 243 nm.
[c]λ = wavelength.
[d]ϵ = molar coefficient of absorption (molar extinction coefficient).

TABLE 2—*Results of toxicologic analysis.*

Case	Drug	Liver, mg/100 mg	Stomach, mg	Bile, mg/100 mL	Urine, mg/100 mL
1	colchicine	0.1	3	0.32	NA[a]
1	lumicolchicine[b]	...	present	...	...
2	colchiceine[c] (desmethyl colchicine)	0.33	present	NA	1.25

[a]NA = none available.

[b]Although no standard was available for analysis, it is believed that the substance was lumicolchicine. The R_f value is consistent with that reported by Stahl [*12*]. The compound was produced when colchicine was exposed to light, particularly in methanolic solution, and so it was necessary to protect such solutions from the light.

[c]Colchicine is converted to colchiceine by acid hyrolysis and readily forms a jade-green color with ferric chloride solution [*7*].

Conclusion

It would seem that both subjects were aware of the toxic nature of colchicine. Suicide was achieved by ingesting many times the lethal limit. The subject of Case 1 chose a rather unusual method of consuming his poison, using beer as a chaser. He evidently also thought that a large quantity of prednisone added to the drink would be effective. After ingesting a large quantity of the tablets, the subject of Case 2 had second thoughts about the suicide as he began to feel the toxic effects. This particular case was toxicologically unusual because the colchicine was present in the hydrolyzed form, colchiceine, possibly because of the prolonged period between ingestion and death.

In general, colchicine is not readily available except on prescription for the treatment of gout. It is seldom used in suicide. The prolonged toxic effects, gastrointestinal disturbances, and other effects, if known, would probably be deterrents.

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