

Schriftliche Prüfungen

Semesterkurs Analytik V

Analytical Strat.

Winter 2010/11

MSc CHAB

Vorname: _____ Name: _____

- Es sind alle Aufgaben zu lösen. Jede Aufgabe wird separat benotet.
- **Zeit: 60 Min.** Teilen Sie sich Ihre Zeit gut ein.
- Es sind alle Hilfsmittel mit Ausnahme von Computern und Telekommunikation erlaubt.
- Unleserliche Texte, unklare Formulierungen oder unsaubere Skizzen können nicht bewertet werden. Bitte bemühen Sie sich um eine saubere Darstellung.
- Beginnen Sie jede Aufgabe auf einem neuen Blatt und schreiben Sie jedes abzugebende Blatt einzeln mit Ihrem Namen und Vornamen an.
- Dieses Deckblatt ist ausgefüllt abzugeben. Die Aufgabenstellung ist ebenfalls einzureichen.
- Wir bitten Sie um Fairness und wünschen Ihnen viel Erfolg!

A case of emergency in the hospital: The patient shows symptoms of a poisoning (vomiting, nausea and diarrhea). When he reports that he had salad with bear's garlic for lunch about 6 hours ago, the medical doctors assume an intoxication of

colchicine. This alkaloid is present in meadow saffron (“Herbstzeitlose”), a plant with a similar appearance to bear’s garlic (see pictures below).

You are responsible for the analytical laboratory in the clinic, and you have to prove the suspicion of the medical doctors.

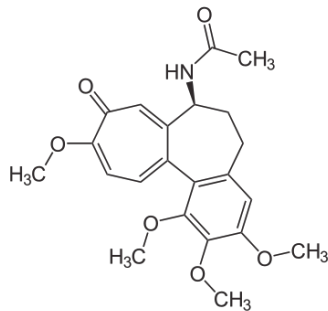
- 1) What kind of sample(s) would you chose for analysis. Describe the sample pretreatment.
- 2) Which would you think is the standard method in a hospital used to determine colchicine? Explain the method in detail. Make some statements about the time required for the analysis, sensitivity of the method and the interpretation of results (negative results, false-positive results). Can you think of other analytical methods as alternatives?
- 3) Colchicin is a therapeutic agent administered to patients suffering from gout arthritis. To find the best dose and therapy for a drug, it is important to have exact knowledge about its metabolisms in the body, including the kinetics. Make suggestions to investigate colchicin metabolism. Consider, what could be a metabolic product?

! NOTE THE INFORMATION GIVEN BELOW!



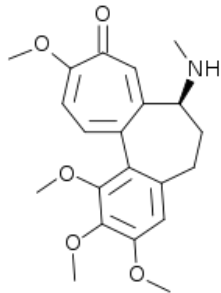
Meadow saffron (left) and bear’s garlic (right).

Some information about colchicine:
Molecular formula:

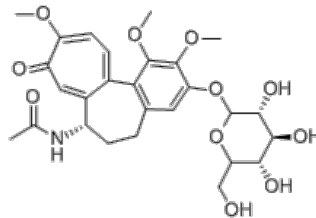


Colchicine is an alkaloid of plant origin. Content of colchicine in meadow saffron: flower (1.8 weight-%), seed (0.5 %), corm (0.2 %), leaves (0.03 %).

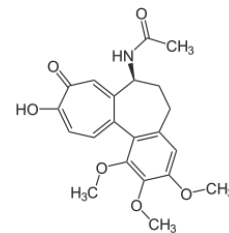
Examples of alkaloids in meadow saffron in lower concentration and with lower toxicity:



Demecolcin
(Desacetylmethylcolchicine)



Colchicoside



Colchiceine

Colchicine impedes cell division in animal cells, and results in abnormal cell division in plant cells. Lethal dose (humans): 2-60 mg (ca. 0.8 mg/kg), depending on weight and health status. Symptoms of poisoning are far below the lethal dose.

Medical use: Colchicine is used in veterinary medicine to treat papillomas and warts in cattle and horses, and in human medicine in the therapy of gout arthritis. Example of a treatment after an acute gout shock: 1 or 1.3 mg initial dose, followed by 0.5 to 0.65 mg every 1 to 2 hours (or 1 to 1.3 mg every 2 hours) until the pain is relieved or nausea and diarrhoea appear. The total dose should not exceed 10 mg over 3 days.

Distribution and metabolism:

In patients with poisoning symptoms, concentrations between 4 – 66 µg/L have been detected in blood, erythrocytes, or plasma. Higher concentrations were found in postmortem tissues of liver, heart, and kidney ranging from 347 – 575 µg/kg, and in bile (2.9-12 mg/L).

Colchicine is secreted unchanged (20-50 %, depending on the uptake) or as metabolites. It undergoes some hepatic metabolism. Large amounts of colchicine and of its metabolites undergo enterohepatic circulation. This may explain the occurrence of a second plasma peak concentration observed 5 to 6 hours after ingestion.