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Ipecac

DEFINITION

Ipecac consists of the dried rhizome and roots of *Cephaëlis acuminata* Karsten, or of *Cephaëlis ipecacuanha* (Brotero) A.Richard (Fam. Rubiaceae). Ipecac yields NLT 2.0% of the total ether-soluble alkaloids of ipecac. Its content of emetine ($C_{29}H_{40}N_2O_4$) and cephaeline ($C_{28}H_{38}N_2O_4$) together is NLT 90.0% of the amount of the total ether-soluble alkaloids. The content of cephaeline varies from an amount equal to, to an amount NMT 2.5 times, the content of emetine.

COMPOSITION

• **Total Ether-Soluble Alkaloids**

[Note—It is important that the ether used in this *Assay* must have been shown by test to be free from peroxides within 24 h before use.]

The alkaloids may be extracted by either of the methods given below.

Method 1

Sample solution: To 10 g of finely powdered Ipecac, in a suitable container, add 100 mL of ether, accurately measured at 25°, insert the stopper in the container tightly, shake the mixture thoroughly, and allow to stand for 5 min. Add 10 mL of 6 N ammonium hydroxide, close again tightly, shake it for 1 h in a mechanical shaker or intermittently during 2 h, and allow to stand overnight at a temperature not exceeding 25°. Again shake the mixture intermittently during 30 min, and allow the drug to settle at 25°. Transfer to a separator a 50.0-mL aliquot of the clear supernatant, representing 5 g of Ipecac.

Method 2

Sample solution: Place 5 g of the finely powdered Ipecac in a continuous-extraction thimble. Add enough ether to cover the powder, and allow to stand for 10 min with occasional stirring. Add 3 mL of ammonium hydroxide, mix, and allow to stand overnight. Cover the drug with a pledget of cotton, pack well, and extract with ether for 5 h. Transfer the ether extract to a separator.

Analysis: Extract the alkaloids from the ether with 2 N sulfuric acid, using at first 15 mL, or more if necessary, to ensure an acid reaction, then successive 10-mL portions until extraction is complete, and filtering all extracts through the same filter into a second separator. To the combined acid solutions add an equal volume of ether, render the mixture distinctly alkaline with 6 N ammonium hydroxide (at least pH 10, by test paper), and extract with successive portions of ether until the last extract shows NMT a slight turbidity when treated as follows: Evaporate 1 mL of the last extraction, dissolve the residue in 0.5 mL of 0.5 N hydrochloric acid, and add 1 drop of mercuric iodide TS.

Filter each portion of the ether extract into a flask or beaker, and carefully evaporate the combined ether extracts on a steam bath almost to dryness. Add 5 mL of ether and 10.0 mL of 0.1 N sulfuric acid VS, and heat on a steam bath to dissolve the alkaloids and to remove all of the ether. Cool, add 15 mL of water, then add methyl red TS, and titrate the excess acid with 0.1 N sodium hydroxide VS. Each mL of 0.1 N sulfuric acid is equivalent to 24.0 mg of the total ether-soluble alkaloids of ipecac, calculated as emetine ($C_{29}H_{40}N_2O_4$).

Acceptance criteria: NLT 2.0%

• **Emetine and Cephaeline**

Solution A: Prepare 0.5 M monobasic potassium phosphate (containing 5.1 g/75 mL) and 0.5 M dibasic potassium phosphate (containing 2.2 g/25 mL). Mix three volumes of 0.5 M monobasic potassium phosphate with one volume of 0.5 M dibasic potassium phosphate, and adjust by the addition of one or the other of the solutions to a pH of 6.0 ± 0.05. Dissolve 7.5 g of potassium chloride in 100 mL of the resulting solution.

Solution B: 0.5 M sodium citrate (containing 6.5 g/50 mL) and citric acid (containing 4.8 g/50 mL). Mix equal volumes of these solutions, and adjust by the addition of one or the other of the solutions to a pH of 4.0 ± 0.05.

Standard solution: 50 µg/mL of emetine from USP Emetine Hydrochloride RS in 0.5 N sulfuric acid

Sample solution: Transfer 200 mg of the fine powder to a 150-mL beaker. Add 2 mL of dimethyl sulfoxide, mix with a flattened stirring rod to ensure complete wetting of the powder, and allow to stand for 30 min. Add 2 mL of water and 1 g of sodium bicarbonate.

Chromatographic columns: For each column, pack a pledget of fine glass wool in the base of a chromatographic tube (25- × 200-mm test tube to which is fused a 5-cm length of 7-mm tubing) with the aid of a tamping rod having a disk with a diameter 1 mm less than that of the tube.

Column I: Prepare *Column I* as follows. To the *Sample solution* add 6 g of purified siliceous earth, mix, transfer the mixture to the column, scrub the beaker with 1 g of the purified siliceous earth, transfer this to the top of the column, and tamp.

Column II: Prepare *Column II* using 3 g of the purified siliceous earth and 2 mL of *Solution A*.

Column III: Prepare *Column III* using 2 mL of *Solution B* and 3 g of the purified siliceous earth.

Column IV: Prepare *Column IV* using 2 mL of sodium hydroxide solution (1 in 50) and 3 g of the purified siliceous earth.

Pack a pledget of glass wool on the top of each column.

Analysis

[NOTE—Use water-saturated solvents throughout this *Analysis*. Rinse the tips of the chromatographic columns before discarding them.]

Emetine solution: Mount *Columns I* and *II* so that the effluent from *Column I* flows onto *Column II*. Pass three 50-mL portions of ether through the columns, and discard *Column I* and the eluate. Mount *Column III* below *Column II* and pass three 50-mL portions of a mixture of one volume of ether and three volumes of chloroform through the columns. Discard *Column II* and the eluate. Wash *Column III* with 25 mL of the ether–chloroform mixture, followed by 25 mL of a mixture of equal volumes of ether and isooctane, and discard the washings. Wash *Column IV* with 20 mL of a 1-in-50 solution of triethylamine in the ether–isooctane mixture, and discard the washing. Mount *Column IV* below *Column III*, and place as a receiver under *Column IV* a 125-mL separator containing 15 mL of 4 N sulfuric acid. Pass through the columns 10 mL of a 1-in-5 solution of triethylamine in the ether–isooctane mixture, followed by three 10-mL portions of a 1-in-50 solution of triethylamine in the ether–isooctane mixture. Discard *Column III*, and pass through *Column IV* 20 mL of the 1-in-50 solution of triethylamine in the ether–isooctane mixture. Shake the separator, allow the phases to separate, and transfer the aqueous extract to a 50-mL volumetric flask. Extract with two additional 10-mL portions of 0.5 N sulfuric acid, combining the extracts in the volumetric flask. Add 0.5 N sulfuric acid to volume.

Cephaeline solution: Elute *Column IV* with 75 mL of chloroform, collecting the eluate in a 250-mL separator containing 150 mL of ether. Discard *Column IV*. Extract with one 20-mL and then with two 10-mL portions of 0.5 N sulfuric acid, collecting the extracts in a 50-mL volumetric flask. Rinse the stem of the separator, and add the acid to volume.

Instrumental conditions

(See *Ultraviolet-Visible Spectroscopy* ⟨857⟩.)

Mode: UV-Vis

Analytical wavelengths: 283 and 350 nm

Cell: 1 cm

Blank: 0.5 N sulfuric acid

Analysis

Samples: *Standard solution, Emetine solution,* and *Cephaeline solution*

Calculate the percentage of emetine in the portion of Ipecac taken:

$$\text{Result} = (A_U/A_S) \times (C_S/C_U) \times 100$$

A_U = difference in the absorbances of the emetine solution from the *Sample solution* at the wavelengths indicated by $(A_{283} - A_{350})$

A_S = difference in the absorbances of the emetine solution from the *Standard solution* at the wavelengths indicated by $(A_{283} - A_{350})$

C_S = concentration of emetine in the *Standard solution* (µg/mL)

C_U = nominal concentration of emetine in the *Sample solution* (mg/mL)

Calculate the percentage of cephaeline in the portion of Ipecac taken:

$$\text{Result} = (A_U/A_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

A_U = difference in the absorbances of the cephaeline solution from the *Sample solution* at the wavelengths indicated by $(A_{283} - A_{350})$

A_S = difference in the absorbances of the cephaeline solution from the *Standard solution* at the wavelengths indicated by $(A_{283} - A_{350})$

C_S = concentration of emetine in the *Standard solution* (µg/mL)

C_U = nominal concentration of cephaeline in the *Sample solution* (mg/mL)

M_{r1} = molecular weight of cephaeline, 466.61

M_{r2} = molecular weight of emetine, 480.64

Acceptance criteria: The content of emetine ($C_{29}H_{40}N_2O_4$) and cephaeline ($C_{28}H_{38}N_2O_4$) together is NLT 90.0% of the total amount of the ether-soluble alkaloids. The content of cephaeline varies from an amount equal to, to an amount NMT 2.5 times, the content of emetine.

CONTAMINANTS

• **ARTICLES OF BOTANICAL ORIGIN** ⟨561⟩, *Pesticide Residue Analysis*: Meets the requirements

SPECIFIC TESTS

• **BOTANICAL CHARACTERISTICS**

Macroscopic: A mixture of segments of the roots and rhizomes. The root segments are mostly curved and flexuous, occasionally branched, up to 15 cm in length and usually 3–6.5 mm in diameter, but may be up to 9 mm in diameter, grayish, grayish brown, or reddish brown, the

reddish brown type often having light-colored abrasions, transverse ridges 0.5–1.0 mm wide that extend halfway around the circumference of the root and fade at their tapering extremities into the general surface, with from one to six of these ridges per centimeter, and annulations sometimes seen at irregular intervals. The rhizomes are cylindrical, 2 mm thick, finely longitudinally wrinkled, with a few elliptical scars. The odor is distinctive; the dust is sternutatory.

Microscopic: At the center of the root is a well-defined primary xylem but no pith. Surrounding this is a dense wood of secondary xylem crossed by medullary rays. These elements are all lignified. External to the wood is a narrow band of secondary phloem and a wide parenchymatous phelloderm surrounded by a narrow layer of cork a few cells thick. The secondary xylem consists of narrow, bordered-pitted tracheidal vessels and tracheids in combination with xylem parenchyma. The latter have simple pits and contain starch grains. Starch is present also in the medullary rays. The phloem occurs as small groups of sieve tissue embedded in parenchyma. The wide phelloderm consists of round-celled cellulose parenchyma filled with starch grains and a few idioblasts, each of which contains a bundle of acicular raphides of calcium oxalate crystals 30- to 80-µm long. The starch grains are rarely single but usually occur as 2–4 and sometimes 8 in a clump. Individual grains measure up to 22 µm in diameter.

The rhizome differs from the root in having a ring of xylem around a large pith. The pericycle contains characteristic sclerenchymatous cells. Spiral vessels are found in the protoxylem. The pith is composed of pitted parenchyma, which is somewhat lignified.

- **Overground Stems:** The proportion of overground stems is NMT 5%.
- **Articles of Botanical Origin ⟨561⟩, *Methods of Analysis, Foreign Organic Matter*:** The proportion of foreign organic matter is NMT 2.0%.

ADDITIONAL REQUIREMENTS

- **USP Reference Standards ⟨11⟩**

USP Emetine Hydrochloride RS

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
IPECAC	Nam-Cheol Kim Scientific Liaison	BDSHM2020 Botanical Dietary Supplements and Herbal Medicines
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	BDSHM2020 Botanical Dietary Supplements and Herbal Medicines

Chromatographic Database Information: Chromatographic Database

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