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Paregoric

DEFINITION

Paregoric contains NLT 35 mg and NMT 45 mg of anhydrous morphine in each 100 mL.

Prepare Paregoric as follows.

Powdered Opium	4.3 g
Suitable Essential Oil(s)	—
Benzoic Acid	3.8 g
Diluted Alcohol	900 mL
Glycerin	38 mL
To make	950 mL

Prepare a diluted alcohol mixture containing 400 mg of *Benzoic Acid*, 4 mL of *Glycerin*, and sufficient *Suitable Essential Oil(s)* in each 100 mL of *Diluted Alcohol*. Separately, macerate the *Powdered Opium*, *Benzoic Acid*, and *Suitable Essential Oil(s)* for 5 days, with occasional agitation, in a mixture of *Diluted Alcohol* and *Glycerin*. Then filter, and pass enough *Diluted Alcohol* through the filter to obtain 950 mL of total filtrate. Assay a portion of this filtrate as directed herein, and dilute the remainder with a sufficient quantity of the previously prepared diluted alcohol mixture to yield a solution containing 40 mg of anhydrous morphine in each 100 mL.

Paregoric may also be prepared by using Opium or Opium Tincture instead of *Powdered Opium*, the anhydrous morphine content being adjusted to 40 mg in each 100 mL and the alcohol content being adjusted to 45%.

ASSAY

• **Procedure**

Mobile phase A: 1-in-5 solution of triethylamine in water-saturated chloroform

Mobile phase B: 1-in-100 solution of triethylamine in water-saturated chloroform

Chromatographic tubes: Prepare three similar tubes, each about 260 mm long and consisting of about 200 mm of 25-mm tubing and about 6 cm of 6-mm tubing. In each of the tubes, place a pledget of glass wool at a point where the 6-mm tubing is constricted slightly, about 2 cm from the junction.

Citrate buffer: 0.1 M sodium citrate and 0.1 M citric acid (50:50)

Standard solution: Dissolve a quantity of USP Morphine Sulfate RS equivalent to about 40 mg of anhydrous morphine in 0.5 mL of triethylamine contained in a 100-mL volumetric flask, and add methanol to volume. Pipet 10 mL of this solution into a 50-mL volumetric flask, add 1 mL of triethylamine and 1 mL of hydrochloric acid, and add water-saturated chloroform to volume.

Sample solution: Evaporate 10.0 mL of Paregoric (equivalent to about 4 mg of morphine) on a steam bath under a stream of air to about 2 mL, and cool. [Note—Avoid reducing the volume to less than 2 mL.] Add 0.5 mL of *Citrate buffer*.

Chromatographic columns: Fill the three tubes with adsorbent prepared as follows, using chromatographic siliceous earth as the base of the adsorbent, and tamp it firmly in place. After filling, place a small pad of glass wool above each column packing.

Column I: Pack in two layers, the lower layer consisting of 3 g of chromatographic siliceous earth mixed with 2 mL of *Citrate buffer* and the upper layer of 3 g of chromatographic siliceous earth mixed with the *Sample solution*. Dry-rinse the beaker in which the components of the two layers have been mixed with 1 g of chromatographic siliceous earth, and add it also to the top of the column.

Column II: Pack with 3 g of chromatographic siliceous earth mixed with 2 mL of dibasic potassium phosphate solution (1 in 5.75).

Column III: Pack with 3 g of chromatographic siliceous earth mixed with 2 mL of sodium hydroxide solution (1 in 50).

Instrumental conditions

Mode: UV-Vis

Analytical wavelength: 255–360 nm

Cell: 1 cm

Blank: Chloroform

Analysis

[NOTE—(1) Use water-saturated solvents throughout this procedure; (2) prepare eluants fresh daily; and (3) avoid bringing the solutions into contact with metal.]

Wash *Column I* with 100 mL of ether, followed by 100 mL of chloroform. Rinse the tip of the column with chloroform, and discard the solvents. In the following operations, rinse each column tip before discarding the column or changing receivers.

Mount the three columns vertically so that the effluent from *Column I* flows into *Column II*, and the effluent from the latter flows into *Column III*. Pass through the three columns 5 mL of *Mobile phase A,* followed by four 10-mL portions of *Mobile phase B,* allowing each portion to pass through completely before subsequent additions. Discard *Column I*.

Pass three 5-mL portions of *Mobile phase B* through the two remaining columns. Discard *Column II*.

Wash *Column III* successively with 10 mL of *Mobile phase B*, 50 mL of chloroform, 2 mL of a 1-in-10 solution of glacial acetic acid in chloroform, and 50 mL of a 1-in-100 solution of glacial acetic acid in chloroform. Discard all washings. Arrange to collect eluate from *Column III* in a 50-mL volumetric flask containing 10 mL of methanol and 1 mL of hydrochloric acid. Elute the column with 5 mL of *Mobile phase A,* followed by 33 mL of *Mobile phase B*. Dilute with chloroform to volume, and mix.

Concomitantly record the spectra of this solution and the *Standard solution,* and plot the corresponding wavelength-absorbance curves. Correct the absorbance of each solution, at the wavelength of maximum absorbance at about 285 nm, by extrapolating the portion of the base-line curve between 340 and 310 nm to this wavelength.

Calculate the weight of anhydrous morphine, in mg, in 100 mL of Paregoric taken:

$$\text{Result} = (A_U/A_S) \times W \times F$$

A_U = corrected absorbance of the *Sample solution*

A_S = corrected absorbance of the *Standard solution*

W = weight of anhydrous morphine in the 50 mL of *Standard solution* (mg)

F = dilution factor, 10

Acceptance criteria: 35–45 mg of anhydrous morphine per 100 mL of Paregoric

OTHER COMPONENTS

• **ALCOHOL DETERMINATION,** *Method II*⟨611⟩**:** 43.0%–47.0% of C_2H_5OH, using acetone as the internal standard

ADDITIONAL REQUIREMENTS

• **PACKAGING AND STORAGE:** Package in tight, light-resistant containers, and avoid exposure to direct sunlight and to excessive heat.

• **USP REFERENCE STANDARDS** ⟨11⟩

USP Morphine Sulfate RS

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

Topic/Question	Contact	Expert Committee
PAREGORIC	Nam-Cheol Kim Scientific Liaison	CMP2020 Compounding 2020
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	CMP2020 Compounding 2020

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. Information currently unavailable

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