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Assay for dextrose—

Periodic acid reagent solution—Dissolve 8.5 g of sodium periodate in 80 mL of 1 *N* sulfuric acid, dilute with water to 100 mL, and mix.

Assay preparation—Decant the supernatant liquid from Sterile Chromic Phosphate P 32 Suspension into a disposable centrifuge tube, and centrifuge. Pipet 1.0 mL of the clear supernatant liquid into a 25-mL volumetric flask, dilute with water to volume, and mix.

Procedure—Pipet 50 mL of *Periodic acid reagent solution* into a 250-mL conical flask, add 3.0 mL of the *Assay preparation*, swirl, cover the flask, and allow to stand at room temperature for 2 hours. Add, in the order named and with rapid stirring, 50 mL of a saturated solution of sodium bicarbonate, 50.0 mL of 0.1 *N* potassium arsenite VS, 4 mL of potassium iodide solution (1 in 5), and 20 g of sodium bicarbonate. Stir the solution at room temperature for 15 minutes. Titrate with 0.1 *N* iodine VS, using 3 mL of starch TS as the indicator. Perform a blank determination, and make any necessary correction. Each mL of 0.1 *N* iodine is equivalent to 1.802 mg of dextrose ($C_6H_{12}O_6$). Not less than 27.0% and not more than 33.0% is found.

Assay for radioactivity—Using a suitable counting assembly (see *Assay, Beta-emitting radionuclides* under *Radioactivity* ⟨821⟩), determine the radioactivity, in MBq (mCi) per mL, of Sterile Chromic Phosphate P 32 Suspension by use of a calibrated system as directed under *Radioactivity* ⟨821⟩.

Sodium Phosphate P 32 Solution

Phosphoric-^{32}P acid, disodium salt.
Dibasic sodium phosphate-^{32}P [*7635-46-3*].

» Sodium Phosphate P 32 Solution is a solution suitable for either oral or intravenous administration, containing radioactive phosphorus (^{32}P) processed in the form of Dibasic Sodium Phosphate from the neutron bombardment of elemental sulfur. Nonradioactive Dibasic Sodium Phosphate may be added during the processing.

Sodium Phosphate P 32 Solution contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of ^{32}P as phosphate expressed in megabecquerels (microcuries or millicuries) per mL at the time indicated in the labeling. Other chemical forms of radioactivity are absent.

Packaging and storage—Preserve in single-dose or in multiple-dose containers that previously have been treated to prevent adsorption.

Labeling—Label it to include the following: the time and date of calibration; the amount of ^{32}P as phosphate expressed in total megabecquerels (microcuries or millicuries) and in megabecquerels (microcuries or in millicuries) per mL at the time of calibration; the name and quantity of any added preservative or stabilizer; a statement of the intended use, whether oral or intravenous; a statement of whether the contents are intended for diagnostic or therapeutic use; the expiration date; and the statements, "Caution—Radioactive Material," and "Not for intracavitary use." The labeling indicates that in making dosage calculations, correction is to be made for radioactive decay, and also indicates that the radioactive half-life of ^{32}P is 14.3 days.

Reference standard—*USP Endotoxin Reference Standard.*

Radionuclide identification—

A: The beta radiation of the Solution, measured according to the procedure set forth under *Radioactivity* ⟨821⟩, shows a mass absorption coefficient within ±5% of the value found for a specimen of a known standard of the same radionuclide when determined under identical counting conditions and geometry.

B: Its beta-ray and/or Bremsstrahlung spectrum is identical to that of a specimen of ^{32}P of known purity showing no distinct photopeaks and no energies greater than 1.710 MeV.

Bacterial endotoxins—It meets the requirements of the *Bacterial Endotoxins Test* ⟨85⟩, the limit of endotoxin content being not more than $175/V$ USP Endotoxin Unit per mL of the Injection, when compared with the USP Endotoxin RS, in which V is the maximum recommended total dose, in mL, at the expiration date or time.

pH ⟨791⟩: between 5.0 and 6.0.

Radiochemical purity—Place a measured volume, appropriately diluted with phosphoric acid solution (1 in 20) such that it provides a count rate of about 20,000 counts per minute, about 45 mm from the end of a 25- × 300-mm strip of chromatographic paper (see *Chromatography* ⟨621⟩), and allow to dry. Develop the chromatogram by descending chromatography, using a mixture of tertiary butyl alcohol, water, and formic acid (40:20:5). Allow to dry, and determine the position of the phosphoric acid by spraying the paper with a solution prepared by dissolving 5 g of ammonium molybdate in 100 mL of water and pouring, with constant stirring, into a mixture of 12 mL of nitric acid and 24 mL of water. Determine the position of the radioactivity distribution by scanning with a collimated radiation detector. The radioactivity appears in one band only, corresponding in R_f value to the phosphoric acid.

Other requirements—Solution intended for intravenous use meets the requirements under *Injections* ⟨1⟩, except that the Solution may be distributed or dispensed prior to completion of the test for *Sterility*, the latter test being started on the day of final manufacture, and except that it is not subject to the recommendation on *Volume in Container*.

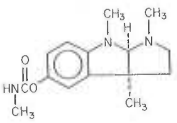
Assay for radioactivity—Using a suitable counting assembly (see *Assay, Beta-emitting radionuclides* under *Radioactivity* ⟨821⟩), determine the radioactivity, in MBq (mCi) per mL, of Sodium Phosphate P 32 Solution by use of a calibrated system as directed under *Radioactivity* ⟨821⟩).

Phosphoric Acid—*see* Phosphoric Acid NF

Phosphoric Acid, Diluted—*see* Phosphoric Acid, Diluted NF

Phosphoric Acid Gel, Sodium Fluoride and—*see* Sodium Fluoride and Phosphoric Acid Gel

Physostigmine



$C_{15}H_{21}N_3O_2$ 275.35
Pyrrolo[2,3-*b*]indol-5-ol, 1,2,3,3a,8,8a-hexahydro-1,3a,8-trimethyl-, methylcarbamate (ester), (3a*S-cis*).
Physostigmine.
1,2,3,3aβ,8,8aβ-Hexahydro-1,3a,8-trimethylpyrrolo[2,3-*b*]indol-5-yl methylcarbamate [*57-47-6*].

» Physostigmine is an alkaloid usually obtained from the dried ripe seed of *Physostigma venenosum* Balfour (Fam. Leguminosae). It contains not less than 97.0 percent and not more than 102.0 percent of $C_{15}H_{21}N_3O_2$, calculated on the dried basis.

Packaging and storage—Preserve in tight, light-resistant containers.

Reference standard—*USP Physostigmine Salicylate Reference Standard*—Use without drying.

Identification—It meets the requirements of the test for *Identification—Organic Nitrogenous Bases* ⟨181⟩, USP Physostigmine Salicylate RS being used, and 1 g of sodium bicarbonate being used in place of the 2 mL of 1 *N* sodium hydroxide specified.

Specific rotation ⟨781⟩: between −236° and −246°, measured at 365 nm, calculated on the dried basis, determined in a solution in methanol containing 100 mg in each 10 mL.

Loss on drying ⟨731⟩—Dry it over silica gel for 24 hours: it loses not more than 1.0% of its weight.

Residue on ignition ⟨281⟩: negligible, from 100 mg.

Readily carbonizable substances ⟨271⟩—Dissolve 100 mg in 5 mL of sulfuric acid TS: at the end of 5 minutes the solution has no more color than Matching Fluid I.

Assay—Dissolve about 175 mg of Physostigmine, accurately weighed, in 25 mL of chloroform. Add 25 mL of glacial acetic acid, and titrate with 0.02 *N* perchloric acid in dioxane VS, determining the end-point potentiometrically. Perform a blank determination, and make any necessary correction. Each mL of 0.02 *N* perchloric acid is equivalent to 5.507 mg of $C_{15}H_{21}N_3O_2$.

Physostigmine Salicylate

$C_{15}H_{21}N_3O_2.C_7H_6O_3$ 413.47

Pyrrolo[2,3-*b*]indol-5-ol, 1,2,3,3a,8,8a-hexahydro-1,3a,8-trimethyl-, methylcarbamate (ester), (3a*S*-*cis*)-, mono-(2-hydroxybenzoate).

Physostigmine monosalicylate [*57-64-7*].

» Physostigmine Salicylate contains not less than 97.0 percent and not more than 102.0 percent of $C_{15}H_{21}N_3O_2.C_7H_6O_3$, calculated on the dried basis.

Packaging and storage—Preserve in tight, light-resistant containers.

Reference standard—*USP Physostigmine Salicylate Reference Standard*—Use without drying.

Identification—

A: It responds to the *Identification test* under *Physostigmine.*

B: It responds to the tests for *Salicylate* ⟨191⟩.

Specific rotation ⟨781⟩: between −91° and −94°, calculated on the dried basis, determined in a solution containing 100 mg in each 10 mL.

Loss on drying ⟨731⟩—Dry it over silica gel for 24 hours: it loses not more than 1.0% of its weight.

Residue on ignition ⟨281⟩: negligible, from 100 mg.

Sulfate—Precipitate the salicylic acid from 10 mL of a cold, saturated solution of Physostigmine Salicylate with a slight excess of 3 *N* hydrochloric acid, filter, and to the filtrate add 5 drops of barium chloride TS: no turbidity is produced immediately.

Readily carbonizable substances ⟨271⟩—Dissolve 100 mg in 5 mL of sulfuric acid TS: at the end of 5 minutes the solution has no more color than Matching Fluid I.

Assay—Dissolve about 250 mg of Physostigmine Salicylate, accurately weighed, in 25 mL of chloroform. Add 25 mL of glacial acetic acid, and titrate with 0.02 *N* perchloric acid in dioxane VS, determining the end-point potentiometrically. Perform a blank determination, and make any necessary correction. Each mL of 0.02 *N* perchloric acid is equivalent to 8.270 mg of $C_{15}H_{21}N_3O_2.C_7H_6O_3$.

Physostigmine Salicylate Injection

» Physostigmine Salicylate Injection is a sterile solution of Physostigmine Salicylate in Water for Injection. It contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of $C_{15}H_{21}N_3O_2.C_7H_6O_3$. It may contain an antimicrobial agent and an antioxidant.

Note—Do not use the Injection if it is more than slightly discolored.

Packaging and storage—Preserve in single-dose containers, preferably of Type I glass, protected from light.

Reference standard—*USP Physostigmine Salicylate Reference Standard*—Use without drying.

Identification—

A: It responds to the *Identification test* under *Physostigmine.*

B: It responds to the tests for *Salicylate* ⟨191⟩.

Pyrogen—It meets the requirements of the *Pyrogen Test* ⟨151⟩.

pH ⟨791⟩: between 3.5 and 5.0.

Other requirements—It meets the requirements under *Injections* ⟨1⟩.

Assay—

0.05 M Ammonium acetate—Dissolve 3.85 g of ammonium acetate in 1 liter of water, and adjust, if necessary, with glacial acetic acid or ammonium hydroxide to a pH of 6 ± 0.1.

Mobile phase—Prepare a filtered and degassed mixture of equal volumes of acetonitrile and *0.05 M Ammonium acetate.* Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Benzyl alcohol–benzaldehyde solution—Prepare a mixture of 100 µL of benzyl alcohol and 1 µL of benzaldehyde in each 400 mL of acetonitrile.

Standard preparation—Dissolve an accurately weighed quantity of USP Physostigmine Salicylate RS in *Benzyl alcohol–benzaldehyde solution,* and dilute quantitatively, and stepwise if necessary, with *Benzyl alcohol–benzaldehyde solution,* to obtain a solution having a known concentration of about 30 µg per mL.

Assay preparation—Transfer an accurately measured volume of Physostigmine Salicylate Injection, equivalent to about 3 mg of physostigmine salicylate, to a 100-mL volumetric flask, dilute with acetonitrile to volume, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 254-nm detector and a 3.9-mm × 30-cm column that contains packing L1. The flow rate is about 2 mL per minute. Separately chromatograph 10-µL portions of the *Benzyl alcohol–benzaldehyde solution* and the *Standard preparation,* and record the peak responses as directed under *Procedure* [NOTE—If the components of the *Benzyl alcohol–benzaldehyde solution* co-elute, the *Standard preparation* will exhibit only 2 peaks instead of 3.]: in a suitable system, benzyl alcohol and benzaldehyde elute before physostigmine, the column efficiency determined from the analyte peak is not less than 1200 theoretical plates, the resolution, *R*, between the physostigmine peak and the adjacent peak (benzyl alcohol or benzaldehyde or the combination of these) is not less than 2.0, and the relative standard deviation for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 10 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the quantity, in mg, of $C_{15}H_{21}N_3O_2.C_7H_6O_3$ in each mL of the Injection taken by the formula:

$$0.1(C/V)(r_U/r_S),$$

in which C is the concentration, in µg per mL, of USP Physostigmine Salicylate RS in the *Standard preparation,* V is the volume, in mL, of Injection taken, and r_U and r_S are the peak responses obtained from the *Assay preparation* and the *Standard preparation,* respectively.

Physostigmine Salicylate Ophthalmic Solution

» Physostigmine Salicylate Ophthalmic Solution is a sterile, aqueous solution of Physostigmine Salicylate. It contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of $C_{15}H_{21}N_3O_2.C_7H_6O_3$. It may contain suitable antimicrobial agents, buffers, and stabilizers, and suitable additives to increase its viscosity.