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Perphenazine and Amitriptyline Hydrochloride Tablets

» Perphenazine and Amitriptyline Hydrochloride Tablets contain not less than 90.0 percent and not more than 110.0 percent of the labeled amounts of perphenazine ($C_{21}H_{26}ClN_3OS$) and amitriptyline hydrochloride ($C_{20}H_{23}N \cdot HCl$).

Packaging and storage—Preserve in well-closed containers.

USP Reference standards ⟨11⟩—
USP Amitriptyline Hydrochloride RS
USP Perphenazine RS

[Note—Throughout the following procedures, protect test or assay specimens, the USP Reference Standard, and solutions containing them, by conducting the procedures without delay, under subdued light, or using low-actinic glassware.]

Identification—Transfer a portion of powdered Tablets, equivalent to about 40 mg of perphenazine, to a 100-mL volumetric flask containing about 50 mL of alcohol. Agitate for 20 minutes, add alcohol to volume, mix, and filter or centrifuge. Separately prepare two Standard solutions containing 0.4 mg per mL of USP Perphenazine RS and USP Amitriptyline Hydrochloride RS, respectively, in alcohol. Separately apply 5 µL of the test solution and 5 µL of each Standard solution to a thin-layer chromatographic plate (see *Chromatography ⟨621⟩*) coated with a 0.25-mm layer of chromatographic silica gel mixture. Develop the chromatogram using a solvent system consisting of a mixture of cyclohexane, ethyl acetate, and diethylamine (85:25:5) until the solvent front has moved about 15 cm. Remove the plate from the developing chamber, air-dry for 20 minutes, and examine the plate under short-wavelength UV light: the R_F values of the principal spots obtained from the test solution correspond to those obtained from the Standard solutions.

Dissolution ⟨711⟩—
Medium: 0.1 N hydrochloric acid; 900 mL.
Apparatus 2: 50 rpm.
Time: 60 minutes.
Procedure—[Note—Due to potential decrease in the recovery of perphenazine when multiple injections are made from a vial, no more than two withdrawals should be made from any single vial.] Determine the amounts of perphenazine and amitriptyline hydrochloride in solution in filtered portions of the solution under test, in comparison with a Standard solution having known concentrations of USP Perphenazine RS and USP Amitriptyline Hydrochloride RS in the same medium, as directed for *Procedure* in the *Assay*.
Tolerances—Not less than 75% *(Q)* of the labeled amounts of perphenazine ($C_{21}H_{26}ClN_3OS$) and amitriptyline hydrochloride ($C_{20}H_{23}N \cdot HCl$) is dissolved in 60 minutes.

Uniformity of dosage units ⟨905⟩: meet the requirements for *Content uniformity* with respect to perphenazine and to amitriptyline hydrochloride.

Assay—
Mobile phase—Prepare a filtered and degassed mixture of water, acetonitrile, methanol, and methanesulfonic acid (490:310:200:2). Make adjustments if necessary (see *System Suitability* under *Chromatography ⟨621⟩*).
Standard preparation—Dissolve an accurately weighed quantity of USP Perphenazine RS in methanol, and dilute quantitatively with methanol to obtain a solution having a known concentration of about 0.8 mg per mL (*Solution P*). Transfer 4*J* mg of USP Amitriptyline Hydrochloride RS to a 50-mL volumetric flask, *J* being the ratio of the labeled amount, in mg, of amitriptyline hydrochloride to the labeled amount, in mg, of perphenazine per Tablet. Add 5.0 mL of *Solution P* and 20 mL of 0.2 N acetic acid, shake, and sonicate to dissolve the USP Reference Standards. Dilute with methanol to volume, and mix. Pipet 25 mL of this solution into a 100-mL volumetric flask, dilute with a mixture of methanol and 0.04 N acetic acid (3:2) to volume, and mix to obtain a *Standard preparation* having known concentrations of about 20 µg of USP Perphenazine RS per mL and about 20*J* µg of USP Amitriptyline Hydrochloride RS per mL.
Assay preparation—Transfer 10 Tablets to a 250-mL volumetric flask, add 100 mL of 0.2 N acetic acid, and shake the mixture until the Tablets have disintegrated. Add methanol to volume, mix, and filter. Dilute an accurately measured volume (V_F mL) of the clear filtrate quantitatively with a mixture of methanol and 0.04 N acetic acid (3:2) to obtain a solution (V_A mL) containing about 20 µg of perphenazine per mL, and filter through a membrane filter.
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 1 mL per minute, and is adjusted until the relative retention times for perphenazine

and amitriptyline are about 1 and 1.5, respectively. Chromatograph the *Standard preparation*, and record the peak responses as directed for *Procedure:* the relative standard deviation is not more than 2.0% for replicate injections, and the resolution, *R,* between perphenazine and amitriptyline is not less than 4.

Procedure—Separately inject equal volumes (about 20 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 perphenazine ($C_{21}H_{26}ClN_3OS$) in each Tablet taken by the formula:

$$0.25(C/10)(V_A/V_F)(r_U/r_S)$$

in which C is the concentration, in µg per mL, of USP Perphenazine RS in the *Standard preparation*, V_A is the volume, in mL, of the *Assay preparation*, V_F is the volume, in mL, of the filtrate taken for the *Assay preparation*, and r_U and r_S are the responses of the perphenazine peaks obtained from the *Assay preparation* and the *Standard preparation*, respectively. Calculate the quantity, in mg, of amitriptyline hydrochloride ($C_{20}H_{23}N \cdot HCl$) taken by the same formula, reading amitriptyline hydrochloride instead of perphenazine.

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

Topic/Question	Contact	Expert Committee
PERPHENAZINE AND AMITRIPTYLINE HYDROCHLORIDE TABLETS	Documentary Standards Support	SM42020 Small Molecules 4
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

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