Status: Currently Official on 15-Feb-2025
Official Date: Official Prior to 2013
Document Type: USP Monographs
DocId: GUID-54FCAB02-B882-42C0-AD33-6C7B4293A971_4_en-US
DOI: https://doi.org/10.31003/USPNF_M38550_04_01
DOI Ref: r5bxc

Hydroflumethiazide Tablets

» Hydroflumethiazide Tablets contain not less than 95.0 percent and not more than 105.0 percent of the labeled amount of hydroflumethiazide ($C_8H_8F_3N_3O_4S_2$).

Packaging and storage—Preserve in tight containers.

USP Reference standards ⟨11⟩—

USP Hydroflumethiazide RS

Identification—Finely powder a number of Tablets, equivalent to about 100 mg of hydroflumethiazide, and place the powder in a 35-mL, screw-capped centrifuge tube. Add 30 mL of acetone, cap the tube, and allow it to stand for 30 minutes, with occasional shaking. Centrifuge, and decant the supernatant into a 100-mL beaker. Evaporate on a steam bath to dryness, add 10 mL of sodium hydroxide solution (1 in 250) to the residue, and mix. Transfer the liquid to a 125-mL separator. Rinse the beaker with 5 mL of water, and add the rinsing to the main portion. Add 50 mL of anhydrous ethyl ether to the separator, insert the stopper, shake vigorously for 2 minutes, releasing pressure as necessary, and allow the phases to separate. Draw off the lower phase, retaining any emulsion in the separator, and pass it through a membrane filter having a 0.2- to 2-µm porality. Add dilute hydrochloric acid (1 in 10) dropwise to the filtrate in a 50-mL beaker, stirring well and checking the pH with wide-range test paper after each drop. [Note—Crystallization begins at about pH 5. Rubbing the bottom of the beaker with a glass stirring rod helps to initiate crystallization.] When precipitation is complete, decant and discard the supernatant, and wash the precipitate with 5 mL of water. Decant and discard the wash water, and dry the precipitate at 105° for 30 minutes: the IR spectrum of a potassium bromide dispersion of the dried material exhibits maxima only at the same wavelengths as that of a similar preparation of USP Hydroflumethiazide RS.

Dissolution ⟨711⟩—

Medium: dilute hydrochloric acid (1 in 100); 900 mL.

Apparatus 2: 50 rpm.

Time: 60 minutes.

Procedure—Determine the amount of $C_8H_8F_3N_3O_4S_2$ dissolved from UV absorbances at the wavelength of maximum absorbance at about 273 nm of filtered portions of the solution under test, suitably diluted with *Dissolution Medium*, if necessary, in comparison with a Standard solution having a known concentration of USP Hydroflumethiazide RS in the same medium.

Tolerances—Not less than 80% *(Q)* of the labeled amount of $C_8H_8F_3N_3O_4S_2$ is dissolved in 60 minutes.

Uniformity of dosage units ⟨905⟩: meet the requirements.

Procedure for content uniformity—Crush 1 Tablet and quantitatively transfer to a 100-mL volumetric flask, add about 50-mL of methanol, and shake until disintegration is complete. Dilute with methanol to volume, mix, and filter, discarding the first 20 mL of the filtrate. Dilute a portion of the subsequent filtrate with methanol to obtain a solution containing approximately 10 µg of hydroflumethiazide per mL. Concomitantly determine the absorbances of this solution and of a Standard solution of USP Hydroflumethiazide RS, in the same medium having a known concentration of about 10 µg per mL in 1-cm cells at the wavelength of maximum absorbance at about 273 nm, with a suitable spectrophotometer, using methanol as the blank. Calculate the quantity, in mg, of $C_8H_8F_3N_3O_4S_2$ in the Tablet taken by the formula:

$$(TC/D)(A_U/A_S)$$

in which T is the labeled quantity, in mg, of hydroflumethiazide in the Tablet; C is the concentration, in µg per mL, of USP Hydroflumethiazide RS in the Standard solution; D is the concentration, in µg per mL, of hydroflumethiazide in the test solution, based upon the labeled quantity per Tablet and the extent of dilution; and A_U and A_S are the absorbances of the solution from the Tablet and the Standard solution, respectively.

Assay—

Standard preparation—Transfer about 30 mg of USP Hydroflumethiazide RS, accurately weighed, to a 100-mL volumetric flask, add sodium hydroxide solution (1 in 100) to volume, and mix. Transfer 5.0 mL of this solution to a second 100-mL volumetric flask, dilute with sodium hydroxide solution (1 in 100) to volume, and mix. The concentration of USP Hydroflumethiazide RS in the *Standard preparation* is about 15 µg per mL.

Chromatographic column—Proceed as directed in *Chromatography ⟨621⟩, General Procedures, Column Chromatography*, packing a chromatographic tube with two segments of packing material. The lower segment is a mixture of 1 g of *Solid Support* and 1 mL of sodium hydroxide solution (1 in 100), and the upper segment is a mixture prepared as directed under *Assay preparation*.

Assay preparation—Weigh and finely powder not less than 20 Tablets. Transfer an accurately weighed portion of the powder, equivalent to about 75 mg of hydroflumethiazide, to a 50-mL volumetric flask, add about 35 mL of sodium hydroxide solution (1 in 100), shake vigorously, dilute with sodium hydroxide solution (1 in 100) to volume, and mix. Mix 2.0 mL of this solution with 3 g of *Solid Support* as directed under *Chromatographic column*, and transfer to the column. Wash the column with 50 mL of water-saturated chloroform, then with 50 mL of water-saturated ether, and discard the eluates. Elute the hydroflumethiazide from the column with 100 mL of glacial acetic acid in ether (1 in 1000), collecting the eluate in a 250-mL separator. Add 100 mL of a 1 in 1000 solution of glacial acetic acid in ether to a second 250-mL separator to provide a blank, and treat each as follows: Add 60 mL of isooctane to each separator, mix, and extract the resulting solution with three 50-mL portions of sodium hydroxide solution (1 in 100), collecting the extracts in a 200-mL volumetric flask. Dilute with sodium hydroxide solution (1 in 100) to volume, and mix.

Procedure—Concomitantly determine the absorbances of the solutions in 1-cm cells at the wavelength of maximum absorbance at about 273 nm, with a suitable spectrophotometer, using the blank. Calculate the quantity, in mg, of hydroflumethiazide ($C_8H_8F_3N_3O_4S_2$) in the portion of Tablets taken by the formula:

$$5C(A_U/A_S)$$

in which C is the concentration, in µg per mL, of USP Hydroflumethiazide RS in the *Standard preparation*; and A_U and A_S are the absorbances of the *Assay preparation* and the *Standard preparation*, respectively.

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

Topic/Question	Contact	Expert Committee
HYDROFLUMETHIAZIDE TABLETS	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

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Current DocID: GUID-54FCAB02-B882-42C0-AD33-6C7B4293A971_4_en-US
Previous DocID: GUID-54FCAB02-B882-42C0-AD33-6C7B4293A971_2_en-US
Previous DocID: GUID-54FCAB02-B882-42C0-AD33-6C7B4293A971_1_en-US
DOI: https://doi.org/10.31003/USPNF_M38550_04_01
DOI ref: r5bxc