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Dimenhydrinate Oral Solution

» Dimenhydrinate Oral Solution contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of dimenhydrinate ($C_{17}H_{21}NO \cdot C_7H_7ClN_4O_2$).

Packaging and storage—Preserve in tight containers.

USP Reference standards ⟨11⟩—
USP Dimenhydrinate RS

Identification—The relative retention times of the major peaks for 8-chlorotheophylline and diphenhydramine in the chromatogram of the *Assay preparation* correspond to those in the chromatogram of the *Standard preparation,* as obtained in the *Assay.*

Change to read:

Content of 8-chlorotheophylline—

Ammonium bicarbonate solution ▲—Dissolve 4 g of ammonium bicarbonate in 250 mL of water.

Diluent—Dissolve 4 g of ammonium bicarbonate in 200 mL of water. Add 50 mL of methanol, and mix.

Solution A—Dissolve 0.8 g of ammonium bicarbonate in 800 mL of water. Add 200 mL of methanol, filter, and degas.

Solution B—Dissolve 0.8 g of ammonium bicarbonate in 150 mL of water. Add 850 mL of methanol, filter, and degas.

Mobile phase—Use variable mixtures of *Solution A* and *Solution B* as directed for *Chromatographic system*. Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Internal standard solution—Prepare a solution in methanol containing 2.0 mg of 2-hydroxybenzyl alcohol per mL.▲ (ERR 1-Nov-2021)

Standard solution—▲Accurately weigh about 50 mg of USP Dimenhydrinate RS, add about 5 mL of *Ammonium bicarbonate solution* and 20.0 mL of *Internal standard solution*, and mix. To 1 mL of this solution add about 9 mL of *Diluent*, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)— The liquid chromatograph is equipped with a 229-nm detector and a 4.6-mm × 25-cm column that contains packing L7. The flow rate is about 1.5 mL per minute. The chromatograph is programmed as follows.

Time (minutes)	Solution A (%)	Solution B (%)	Elution
0	100	0	equilibration
0–7.0	100	0	isocratic
7.0–7.1	100→0	0→100	linear gradient
7.1–15	0	100	isocratic
15–15.1	0→100	100→0	linear gradient
15.1–22.0	100	0	isocratic

Chromatograph the *Standard solution*, and record the peak areas as directed for *Procedure*: the relative retention times are about 0.3 for 8-chlorotheophylline, 0.5 for the internal standard, and 1.0 for diphenhydramine; the resolution, *R*, between 8-chlorotheophylline and the internal standard is not less than 4.5; and the relative standard deviation for replicate injections is not more than 2.0%▲ (ERR 1-Nov-2021)

Test solution—Prepare as directed for *Assay preparation* in the *Assay.*

Procedure—Separately inject equal volumes (about 10 µL) of the *Standard solution* and the *Test solution* into the chromatograph, record the chromatograms, and measure the areas for the major peaks. Calculate the quantity, in mg per mL, of 8-chlorotheophylline ($C_7H_7ClN_4O_2$) in the portion of Oral Solution taken by the formula:

$$(214.61/469.96)(0.05W)(R_U/R_S)$$

in which 214.61 and 469.96 are the molecular weights of 8-chlorotheophylline and dimenhydrinate, respectively; *W* is the weight, in mg, of USP Dimenhydrinate RS in the *Standard solution;* and R_U and R_S are peak area ratios of 8-chlorotheophylline to the internal standard obtained from the *Test solution* and the *Standard solution,* respectively. An amount of 8-chlorotheophylline that is between 43.4% and 47.9% of the amount of dimenhydrinate obtained in the *Assay* is found.

[Alcohol Determination ⟨611⟩](): between 4.0% and 6.0% of C_2H_5OH.

Change to read:

Assay—

Ammonium bicarbonate solution▲—Dissolve 4 g of ammonium bicarbonate in 250 mL of water

Diluent—Dissolve 4 g of ammonium bicarbonate in 200 mL of water. Add 50 mL of methanol, and mix.

Solution A—Dissolve 0.8 g of ammonium bicarbonate in 800 mL of water. Add 200 mL of methanol, filter, and degas.

Solution B—Dissolve 0.8 g of ammonium bicarbonate in 150 mL of water. Add 850 mL of methanol, filter, and degas.

Mobile phase—Use variable mixtures of *Solution A* and *Solution B* as directed for *Chromatographic system*. Make adjustments if necessary (see *System Suitability* under *Chromatography ⟨621⟩*)

Internal standard solution—Prepare a solution in methanol containing 2.0 mg of 2-hydroxybenzyl alcohol per mL.

Standard preparation—Accurately weigh about 50 mg of USP Dimenhydrinate RS, add about 5 mL of *Ammonium bicarbonate solution* and 20.0 mL of *Internal standard solution*, and mix. To 1 mL of this solution add about 9 mL of *Diluent*, and mix.

Chromatographic system (see *Chromatography ⟨621⟩*)— The liquid chromatograph is equipped with a 229-nm detector and a 4.6-mm × 25-cm column that contains packing L7. The flow rate is about 1.5 mL per minute. The chromatograph is programmed as follows.

Time (minutes)	Solution A (%)	Solution B (%)	Elution
0	100	0	equilibration
0–7.0	100	0	isocratic
7.0–7.1	100→0	0→100	linear gradient
7.1–15	0	100	isocratic
15–15.1	0→100	100→0	linear gradient
15.1–22.0	100	0	isocratic

Chromatograph the *Standard preparation*, and record the peak areas as directed for *Procedure*: the relative retention times are about 0.3 for 8-chlorotheophylline, 0.5 for the internal standard, and 1.0 for diphenhydramine; the resolution, *R*, between 8-chlorotheophylline and the internal standard is not less than 4.5; and the relative standard deviation for replicate injections is not more than 2.0%.▲ (ERR 1-Nov-2021)

Assay preparation—Pipet 5.0 mL of Oral Solution into a suitable container, add 5.0 mL of *Internal standard solution*, and mix. Transfer about 1 mL of this solution to a suitable container, add about 5 mL of *Diluent,* and mix.

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 areas for the major peaks.▲ (ERR 1-Nov-2021) Calculate the quantity, in mg per mL, of dimenhydrinate ($C_{17}H_{21}NO \cdot C_7H_7ClN_4O_2$) in the portion of the Oral Solution taken by the formula:

$$0.05W(R_U/R_S)$$

in which *W* is the weight, in mg, of USP Dimenhydrinate RS in the *Standard preparation;* and R_U and R_S are the peak area ratios of diphenhydramine to the internal standard obtained from 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
DIMENHYDRINATE ORAL SOLUTION	Documentary Standards Support	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

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