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Tramadol Hydrochloride and Acetaminophen Compounded Oral Suspension

DEFINITION

Tramadol Hydrochloride and Acetaminophen Compounded Oral Suspension contains NLT 90.0% and NMT 110.0% of the labeled amounts of tramadol hydrochloride ($C_{16}H_{25}NO_2 \cdot HCl$) and acetaminophen ($C_8H_9NO_2$).

Prepare Tramadol Hydrochloride and Acetaminophen Compounded Oral Suspension containing 7.5 mg/mL of tramadol hydrochloride and 65 mg/mL of acetaminophen as follows (see *Pharmaceutical Compounding—Nonsterile Preparations* ⟨795⟩).

Tramadol Hydrochloride and Acetaminophen tablets[a]	750 mg of tramadol hydrochloride and 6500 mg of acetaminophen
Vehicle: a 1:1 mixture of Ora-Sweet[b] (sugar-free) and Ora-Plus,[b] a sufficient quantity to make	100 mL

[a] Ultracet 37.5-mg/325-mg tablets, Ortho-McNeil Pharmaceutical, Inc., Raritan, NJ.

[b] Paddock Laboratories, Minneapolis, MN.

Calculate the required quantity of each ingredient for the total amount to be prepared. Place the required number of *Tramadol Hydrochloride and Acetaminophen tablets* in a suitable mortar, and comminute to a fine powder. Add the *Vehicle* in small portions, and triturate to make a smooth paste. Add increasing volumes of the *Vehicle* to make a tramadol hydrochloride and acetaminophen liquid that is pourable. Transfer the contents of the mortar, stepwise and quantitatively, to a calibrated bottle. Add enough of the *Vehicle* to bring to final volume, and mix well.

ASSAY

• **Tramadol Hydrochloride**

Solution A: 20 mM of phosphoric acid and 4 g/L of sodium 1-hexane sulfonate

Mobile phase: Acetonitrile and *Solution A* (50:50). Filter and degas.

Diluent: Acetonitrile and water (50:50)

Standard solution: 0.15 mg/mL of USP Tramadol Hydrochloride RS in *Diluent*

Sample solution: Shake thoroughly by hand each bottle of Oral Suspension. Prepare 0.15 mg/mL of tramadol hydrochloride from Oral Suspension and *Diluent*, and centrifuge.

Chromatographic system

(See *Chromatography* ⟨621⟩, *System Suitability*.)

Mode: LC

Detector: UV 275 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Column temperature: 30°

Flow rate: 1.0 mL/min

Injection volume: 5 µL

System suitability

Sample: *Standard solution*

[Note—The retention time for tramadol hydrochloride is about 6 min.]

Suitability requirements

Relative standard deviation: NMT 2.0% for replicate injections

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of tramadol hydrochloride ($C_{16}H_{25}NO_2 \cdot HCl$) in the portion of Oral Suspension taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of USP Tramadol Hydrochloride RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of tramadol hydrochloride in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

- **Acetaminophen**

Mobile phase: Acetonitrile and water (70:30). Filter and degas.

Standard solution: 65 µg/mL of USP Acetaminophen RS in *Mobile phase*

Sample solution: Shake thoroughly by hand each bottle of Oral Suspension. Prepare 65 µg/mL of acetaminophen from Oral Suspension and *Mobile phase*, and centrifuge.

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 275 nm

Column: 4.6-mm × 25-cm; 5-µm packing L1

Column temperature: 30°

Flow rate: 1.0 mL/min

Injection volume: 5 µL

System suitability

Sample: *Standard solution*

[Note—The retention time for acetaminophen is about 2 min.]

Suitability requirements

Relative standard deviation: NMT 2.0% for replicate injections

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of acetaminophen ($C_8H_9NO_2$) in the portion of Oral Suspension taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of USP Acetaminophen RS in the *Standard solution* (µg/mL)

C_U = nominal concentration of acetaminophen in the *Sample solution* (µg/mL)

Acceptance criteria: 90.0%–110.0%

SPECIFIC TESTS

- **pH ⟨791⟩:** 3.8–4.8

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Package in tight, light-resistant containers. Store in a refrigerator or at controlled room temperature.
- **Beyond-Use Date:** NMT 90 days after the date on which it was compounded, when stored in a refrigerator or at controlled room temperature
- **Labeling:** Label to indicate that it is to be well shaken before use, and to state the *Beyond-Use Date*.
- **USP Reference Standards ⟨11⟩**

USP Acetaminophen RS

USP Tramadol Hydrochloride RS

Topic/Question	Contact	Expert Committee
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REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	CMP2020 Compounding 2020

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