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Rivastigmine Tartrate Capsules

DEFINITION

Rivastigmine Tartrate Capsules contain an amount of Rivastigmine Tartrate equivalent to NLT 94.0% and NMT 105.0% of the labeled amount of rivastigmine ($C_{14}H_{22}N_2O_2$).

IDENTIFICATION

The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

• **Procedure**

Buffer: 8.6 mg/mL of monobasic ammonium phosphate in water. Adjust with ammonia solution to a pH of 7.0.

Mobile phase: Methanol, acetonitrile, and *Buffer* (15:15:70)

Standard solution: 0.064 mg/mL of USP Rivastigmine Tartrate RS in *Mobile phase*. [Note—Use a small amount of methanol (about 2% of the final volume) to facilitate dissolution before diluting with *Mobile phase* to volume, and use sonication if necessary.]

System suitability solution: 0.01 mg/mL each of USP Rivastigmine Related Compound A RS and USP Rivastigmine Related Compound B RS in *Mobile phase*

Sample solution: Remove as completely as possible the contents of NLT 20 Capsules, and mix. Transfer a weighed portion of the combined contents, equivalent to about 48 mg of rivastigmine, to a 250-mL volumetric flask. Add 25 mL of methanol and 60 mL of *Mobile phase*, and sonicate for 15 min to disperse the contents. Dilute with *Mobile phase* to volume, mix well, and centrifuge. Dilute a portion of the supernatant with *Mobile phase* to obtain a solution having a concentration of 0.038 mg/mL of rivastigmine, based on the label claim.

Chromatographic system

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

Mode: LC

Detector: UV 215 nm

Column: 4.6-mm × 25-cm; 5-µm packing L7

Flow rate: 1.5 mL/min

Injection size: 20 µL

System suitability

Samples: *Standard solution* and *System suitability solution*

[Note—The relative retention times for rivastigmine related compound A, rivastigmine related compound B, and rivastigmine are 0.46, 0.57, and 1.0, respectively.]

Suitability requirements

Resolution: NLT 1.5 between rivastigmine related compound A and rivastigmine related compound B, *System suitability solution*

Column efficiency: NLT 5000 theoretical plates, *Standard solution*

Tailing factor: NMT 2.3, *Standard solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of $C_{14}H_{22}N_2O_2$ in the portion of Capsules taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times 100$$

r_U = peak response of rivastigmine from the *Sample solution*

r_S = peak response of rivastigmine from the *Standard solution*

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

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

M_{r1} = molecular weight of rivastigmine, 250.34

M_{r2} = molecular weight of rivastigmine tartrate, 400.42

Acceptance criteria: 94.0%–105.0%

PERFORMANCE TESTS

• **Dissolution** ⟨711⟩

Test 1

Medium: Water; 500 mL, deaerated

Apparatus 2: 50 rpm, with sinkers, if necessary

Time: 30 min

Buffer, Mobile phase, and **System suitability solution:** Prepare as directed in the *Assay*.

Standard solution: 0.192 mg/mL of USP Rivastigmine Tartrate RS in *Mobile phase*. Further dilute with *Medium* to obtain a solution having a concentration similar to that expected in the *Sample solution*.

Sample solutions: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size, discarding the first few mL.

Chromatographic system and **System suitability:** Proceed as directed in the *Assay*.

[Note—Use an injection size of 100 µL.]

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of $C_{14}H_{22}N_2O_2$ dissolved:

$$\text{Result} = (r_U/r_S) \times C_S \times (M_{r1}/M_{r2}) \times (V/L) \times 100$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of the *Standard solution* (mg/mL)

M_{r1} = molecular weight of rivastigmine, 250.34

M_{r2} = molecular weight of rivastigmine tartrate, 400.42

V = volume of *Medium* (mL), 500

L = Capsule label claim (mg)

Tolerances: NLT 75% (Q) of the labeled amount of $C_{14}H_{22}N_2O_2$ is dissolved.

Test 2: If the product complies with this test, the labeling indicates that the product meets USP *Dissolution Test 2*.

Medium: Deaerated water; 500 mL

Apparatus 2: 75 rpm

Time: 15 min

Buffer and **Mobile phase:** Proceed as directed in the *Assay*.

Standard solution: 0.192 mg/mL of USP Rivastigmine Tartrate RS in *Mobile phase*. Further dilute with *Medium* to obtain a solution having a concentration similar to that expected in the *Sample solution*.

Sample solution: Pass a portion of the solution under test through a suitable filter of 0.45-µm pore size, discarding the first few milliliters.

Chromatographic system: Proceed as directed in the *Assay*. [Note—Use an injection volume of 100 µL.]

System suitability

Sample: *Standard solution*

Suitability requirements

Relative standard deviation: NMT 2.0%

Tailing factor: NMT 2.3

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of rivastigmine ($C_{14}H_{22}N_2O_2$) dissolved:

$$\text{Result} = (r_U/r_S) \times C_S \times (M_{r1}/M_{r2}) \times (V/L) \times 100$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of the *Standard solution* (mg/mL)

M_{r1} = molecular weight of rivastigmine, 250.34

M_{r2} = molecular weight of rivastigmine tartrate, 400.42

V = volume of *Medium* (mL), 500

L = label claim (mg/Capsule)

Tolerances: NLT 80% (Q) of the labeled amount of rivastigmine ($C_{14}H_{22}N_2O_2$) is dissolved.

• **Uniformity of Dosage Units ⟨905⟩:** Meet the requirements

IMPURITIES

Organic Impurities

• **Procedure**

Buffer, Mobile phase, and **System suitability solution:** Prepare as directed in the *Assay*.

Standard solution: 1.6 µg/mL of USP Rivastigmine Tartrate RS in *Mobile phase*

Sample solution: Remove as completely as possible the contents of NLT 20 Capsules, and mix. Transfer a weighed portion of the combined contents, equivalent to 25 mg of rivastigmine, to a 25-mL volumetric flask. Disperse in 10 mL of *Mobile phase*, and sonicate for 15 min. Dilute with *Mobile phase* to volume, mix well, and centrifuge. Use the supernatant.

Chromatographic system: Proceed as directed in the *Assay*.

System suitability

Samples: *System suitability solution* and *Standard solution*

Suitability requirements

Resolution: NLT 1.5 between rivastigmine related compound A and rivastigmine related compound B, *System suitability solution*

Relative standard deviation: NMT 10.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

[Note—Identify the peaks using the relative retention times provided in *Impurity Table 1*.]

Calculate the percentage of each impurity in the portion of Capsules taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times (1/F) \times 100$$

r_U = peak response of each individual impurity from the *Sample solution*

r_S = peak response of rivastigmine from the *Standard solution*

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

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

M_{r1} = molecular weight of rivastigmine, 250.34

M_{r2} = molecular weight of rivastigmine tartrate, 400.42

F = relative response factor (see *Impurity Table 1*)

Acceptance criteria

Individual impurities: See *Impurity Table 1*.

Total impurities: NMT 1.0%

Impurity Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Phenol impurity[a]	0.28	1.6	0.6
Rivastigmine	1.0	1.0	—
Any other individual impurity	—	1.0	0.2
Total impurities	—	—	1.0

[a] (*S*)-3-[1-(Dimethylamino)ethyl]phenol.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight containers, and store at controlled room temperature.
- **Labeling:** When more than one *Dissolution* test is given, the labeling states the *Dissolution* test used only if *Test 1* is not used.
- **USP Reference Standards** ⟨11⟩

USP Rivastigmine Tartrate RS

USP Rivastigmine Related Compound A RS

(+)-Di-(*p*-toluoyl)-D-tartaric acid.

$C_{20}H_{18}O_8$ 386.35

USP Rivastigmine Related Compound B RS

(*RS*)-3-[1-(Dimethylamino)ethyl]phenyl dimethylcarbamate.

$C_{13}H_{20}N_2O_2$ 236.32

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

Topic/Question	Contact	Expert Committee
RIVASTIGMINE TARTRATE CAPSULES	Documentary Standards Support	SM32020 Small Molecules 3
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM32020 Small Molecules 3

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