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Antipyrine and Benzocaine Otic Solution

DEFINITION

Antipyrine and Benzocaine Otic Solution is a solution of Antipyrine and Benzocaine in Glycerin. It contains NLT 90.0% and NMT 110.0% of the labeled amount of antipyrine ($C_{11}H_{12}N_2O$) and benzocaine ($C_9H_{11}NO_2$).

[Note—In the preparation of this Otic Solution, use Glycerin that has a low water content, in order that the Otic Solution may comply with the limit for *Water Determination*. This may be ensured by using Glycerin having a specific gravity of NLT 1.2607, corresponding to a concentration of 99.5%.]

IDENTIFICATION

• **A.** The UV spectrum of the antipyrine and benzocaine peaks of the *Sample solution* exhibit maxima and minima at the same wavelengths as those of the *Standard solution*, as obtained in the *Assay*.

• **B.** The retention times of the major peaks of the *Sample solution* correspond to those of the *Standard solution*, as obtained in the *Assay*.

ASSAY

• **Procedure**

Solution A: 50 mM monobasic potassium phosphate and 0.2% triethylamine. Adjust with 10 N sodium hydroxide to a pH of 7.0.

Solution B: Acetonitrile

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	85	15
20	50	50
23	50	50
23.1	85	15
25	85	15

Diluent: Acetonitrile and water (1:1)

Standard solution: 0.014 mg/mL of USP Benzocaine RS and 0.054 mg/mL of USP Antipyrine RS in *Diluent*

Sample solution: Nominally 0.014 mg/mL of benzocaine and 0.054 mg/mL of antipyrine prepared as follows. Transfer a suitable quantity of Otic Solution to a suitable volumetric flask. Dilute with *Diluent* to volume.

Chromatographic system

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

Mode: LC

Detector: UV 270 nm. For *Identification A*, use a diode array detector in the range of 200–400 nm.

Column: 4.6-mm × 15-cm; 5-µm packing L7

Flow rate: 1 mL/min

Injection volume: 20 µL

System suitability

Sample: *Standard solution*

[Note—See *Table 2* for the relative retention times for antipyrine and benzocaine.]

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of the labeled amount of antipyrine ($C_{11}H_{12}N_2O$) and benzocaine ($C_9H_{11}NO_2$) in the portion of Otic Solution taken:

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

r_U = peak response of antipyrine or benzocaine from the *Sample solution*

r_S = peak response of antipyrine or benzocaine from the *Standard solution*

C_S = concentration of USP Antipyrine RS or USP Benzocaine RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of antipyrine or benzocaine in the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

IMPURITIES

• **Organic Impurities**

Solution A, Solution B, Mobile phase, and **Chromatographic system:** Proceed as directed in the *Assay*.

System suitability solution: 0.1 mg/mL of USP Antipyrine RS and 0.01 mg/mL of USP Antipyrine Related Compound A RS in *Diluent*

Standard solution: 0.001 mg/mL each of USP Benzocaine RS and USP Ethyl 4-Nitrobenzoate RS, and 0.004 mg/mL of USP Antipyrine RS in *Diluent*

Sample solution: Nominally 3.2 mg/mL of antipyrine and 0.8 mg/mL of benzocaine prepared as follows. Transfer a suitable quantity of Otic Solution to a suitable volumetric flask. Dilute with *Diluent* to volume.

System suitability

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

[Note—See *Table 2* for the relative retention times.]

Suitability requirements

Resolution: NLT 2.0 between antipyrine related compound A and antipyrine, *System suitability solution*

Relative standard deviation: NMT 5%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of ethyl 4-nitrobenzoate in the portion of Otic Solution taken:

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

r_U = peak response of ethyl 4-nitrobenzoate from the *Sample solution*

r_S = peak response of ethyl 4-nitrobenzoate from the *Standard solution*

C_S = concentration of USP Ethyl 4-Nitrobenzoate RS in the *Standard solution* (mg/mL)

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

Calculate the percentage of any individual, unspecified degradation product in the portion of Otic Solution taken:

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

r_U = peak response of each individual, unspecified degradation product from the *Sample solution*

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

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

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

Acceptance criteria: See *Table 2*. Disregard any impurity peaks less than 0.1%.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Antipyrine related compound A[a]	0.46	—
Antipyrine	0.53	—

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Benzocaine	1.0	—
Ethyl 4-nitrobenzoate[b]	1.6	0.2
Any individual, unspecified degradation product	—	0.2
Total degradation products[a]	—	2.0

[a] Process impurities are controlled in the drug substance and are not to be reported here. They are not included in the calculation of total impurities.

[b] Specified impurity related to benzocaine.

- **Limit of Aminobenzoic Acid**

Solution A: Glacial acetic acid and water (1:69)

Solution B: Methanol

Mobile phase: See *Table 3*.

Table 3

Time (min)	Solution A (%)	Solution B (%)
0	90	10
10	90	10
10.1	15	85
13	15	85
13.1	90	10
16	90	10

Diluent: *Solution A* and *Solution B* (9:1)

Standard solution: 0.001 mg/mL of USP Aminobenzoic Acid RS in *Diluent*

Sample solution: Nominally 3.2 mg/mL of antipyrine and 0.8 mg/mL of benzocaine prepared as follows. Transfer a suitable quantity of Otic Solution to a suitable volumetric flask. Dilute with *Diluent* to volume.

Chromatographic system

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

Mode: LC

Detector: UV 280 nm

Column: 3.0-mm × 15-cm; 3.5-µm packing L11

Flow rate: 0.4 mL/min

Injection volume: 5 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 2.0

Relative standard deviation: NMT 5.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of aminobenzoic acid in the portion of Otic Solution taken:

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

r_U = peak response of aminobenzoic acid from the *Sample solution*

r_S = peak response of aminobenzoic acid from the *Standard solution*

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

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

Acceptance criteria: NMT 0.2%

SPECIFIC TESTS

• **Water Determination** ⟨921⟩, *Method I*: NMT 1.0%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight, light-resistant containers. Store at controlled room temperature.

• **USP Reference Standards** ⟨11⟩

USP Aminobenzoic Acid RS
p-Aminobenzoic acid.
$C_7H_7NO_2$ 137.14

USP Antipyrine RS

USP Antipyrine Related Compound A RS
3-Methyl-1-phenyl-1*H*-pyrazol-5(4*H*)-one.
$C_{10}H_{10}N_2O$ 174.20

USP Benzocaine RS

USP Ethyl 4-Nitrobenzoate RS
Ethyl *p*-nitrobenzoate.
$C_9H_9NO_4$ 195.17

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

Topic/Question	Contact	Expert Committee
ANTIPYRINE AND BENZOCAINE OTIC SOLUTION	Documentary Standards Support	SM22020 Small Molecules 2
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