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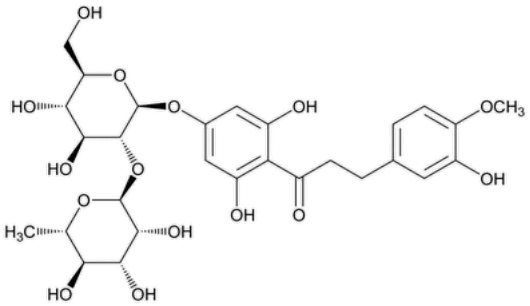
Add the following:

▲Neohesperidin Dihydrochalcone



$C_{28}H_{36}O_{15}$ 612.58

1-Propanone, 1-[4-[[2-*O*-(6-deoxy-α-L-mannopyranosyl)-β-D-glucopyranosyl]oxy]-2, 6-dihydroxyphenyl]-3-(3-hydroxy-4-methoxyphenyl)-;
3,5-Dihydroxy-4-[3-(3-hydroxy-4-methoxyphenyl)propanoyl]phenyl 2-*O*-(α-L-rhamnopyranosyl)-β-D-glucopyranoside CAS RN®: 20702-77-6.

DEFINITION

Neohesperidin Dihydrochalcone contains NLT 96.0% and NMT 102.0% of neohesperidin dihydrochalcone ($C_{28}H_{36}O_{15}$), calculated on the anhydrous basis.

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests** ⟨197⟩, *Infrared Spectroscopy*: **197A**▲ (CN 1-May-2020)

• **B.** 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**

Solution A: 0.5% (v/v) glacial acetic acid in water

Mobile phase: Acetonitrile and *Solution A* (20:80)

Diluent: Dimethyl sulfoxide

System suitability solution: Suspend 100 mg of USP Neohesperidin Dihydrochalcone RS in 10.0 mL of a 100-g/L solution of sulfuric acid in water. Heat the suspension for 5 min on a boiling water bath. Immediately dilute 1.0 mL of the resulting solution with *Diluent* to 50.0 mL. [Note—Neohesperidin dihydrochalcone related compound F and neohesperidin dihydrochalcone related compound G are prepared in situ in this solution.]

Standard solution: 1.0 mg/mL of USP Neohesperidin Dihydrochalcone RS in *Diluent*

Sample solution: 1.0 mg/mL of Neohesperidin Dihydrochalcone in *Diluent*

Chromatographic system

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

Mode: LC

Detector: UV 282 nm

Column: 3.9-mm × 15-cm; 4-µm packing L1, with a carbon loading of 7%

Column temperature: 30°

Flow rate: 1.0 mL/min

Injection volume: 10 µL

Run time: 5 times the retention time of neohesperidin dihydrochalcone

System suitability

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

[Note—For the approximate relative retention times of related substances, see *Table 1*.]

Suitability requirements

Resolution: NLT 2.5 between the neohesperidin dihydrochalcone peak and the neohesperidin dihydrochalcone related compound F peak, *System suitability solution*

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Relative standard deviation: NMT 2.0%, determined from the neohesperidin dihydrochalcone peak, *Standard solution*

Chromatogram similarity: The chromatogram obtained from the *Standard solution* is similar to the reference chromatogram provided with the lot of USP Neohesperidin Dihydrochalcone RS being used.

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of neohesperidin dihydrochalcone ($C_{28}H_{36}O_{15}$) in the portion of Neohesperidin Dihydrochalcone taken:

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

r_U = peak area of neohesperidin dihydrochalcone from the *Sample solution*

r_S = peak area of neohesperidin dihydrochalcone from the *Standard solution*

C_S = concentration of USP Neohesperidin Dihydrochalcone RS in the *Standard solution*

C_U = concentration of Neohesperidin Dihydrochalcone in the *Sample solution*

Acceptance criteria: 96.0%–102.0% on the anhydrous basis

IMPURITIES

- **Residue on Ignition ⟨281⟩:** NMT 0.2%
- **Organic Impurities**

Mobile phase, Diluent, System suitability solution, and **Chromatographic system:** Proceed as directed in the *Assay*.

Standard solution A: Use the *Standard solution*, as prepared in the *Assay*.

Standard solution B: 0.04 mg/mL of USP Neodiosmin RS in *Diluent*

Standard solution C: 0.02 mg/mL of USP Neohesperidin Dihydrochalcone RS from *Standard solution A* in *Diluent*

Sensitivity solution: 0.002 mg/mL of USP Neohesperidin Dihydrochalcone RS from *Standard solution C* in *Diluent*

Sample solution: 2.0 mg/mL of Neohesperidin Dihydrochalcone in *Diluent*

System suitability

Samples: *System suitability solution, Standard solution A, Standard solution C,* and *Sensitivity solution*

[Note—For the approximate relative retention times of related substances, see *Table 1*.]

Suitability requirements

Resolution: NLT 2.5 between the neohesperidin dihydrochalcone peak and the neohesperidin dihydrochalcone related compound F peak, *System suitability solution*

Relative standard deviation: NMT 5.0%, determined from the neohesperidin dihydrochalcone peak, *Standard solution C*

Signal-to-noise ratio: NLT 10, determined from the neohesperidin dihydrochalcone peak, *Sensitivity solution*

Chromatogram similarity: The chromatogram obtained from the *Standard solution A* is similar to the reference chromatogram provided with the lot of USP Neohesperidin Dihydrochalcone RS being used.

Analysis

Samples: *Standard solution B, Standard solution C,* and *Sample solution*

Calculate the percentage of neodiosmin in the portion of Neohesperidin Dihydrochalcone taken:

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

r_U = peak area of neodiosmin from the *Sample solution*

r_S = peak area of neodiosmin from *Standard solution B*

C_S = concentration of USP Neodiosmin RS in *Standard solution B* (mg/mL)

C_U = concentration of Neohesperidin Dihydrochalcone in the *Sample solution* (mg/mL)

Calculate the percentage of each impurity except neodiosmin in the portion of Neohesperidin Dihydrochalcone taken:

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

r_U = peak area of each individual impurity except neodiosmin from the *Sample solution*

r_S = peak area of neohesperidin dihydrochalcone from *Standard solution C*

C_S = concentration of USP Neohesperidin Dihydrochalcone RS in *Standard solution C* (mg/mL)

C_U = concentration of Neohesperidin Dihydrochalcone in the *Sample solution* (mg/mL)

Acceptance criteria: See *Table 1*.

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Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Neohesperidin dihydrochalcone related compound A[a]	0.2	0.5
Neodiosmin[b]	0.38	2.0
Neohesperidin dihydrochalcone related compound C[c]	0.44	0.5
Neohesperidin dihydrochalcone related compound D[d]	0.7	2.0
Neohesperidin dihydrochalcone related compound E[e]	0.8	0.5
Neohesperidin dihydrochalcone	1.0	—
Neohesperidin dihydrochalcone related compound F[f]	1.1	0.5
Neohesperidin dihydrochalcone related compound G[g]	3.4	0.5
Any other individual impurity	—	0.5
Total impurities excluding neodiosmin	—	2.5

[a] 1-[4-[[2-*O*-(6-Deoxy-α-L-mannopyranosyl)-β-D-glucopyranosyl]oxy]-2,6-dihydroxyphenyl]ethanone (phloroacetophenone neohesperidoside).

[b] 7-[[2-*O*-(6-Deoxy-α-L-mannopyranosyl)-β-D-glucopyranosyl]oxy]-5-hydroxy-2-(3-hydroxy-4-methoxyphenyl)-4*H*-1-benzopyran-4-one; 5-Hydroxy-2-(3-hydroxy-4-methoxyphenyl)-4-oxo-4*H*-chromen-7-yl 2-*O*-(α-L-rhamnopyranosyl)-β-D-glucopyranoside.

[c] (2*RS*)-7-[[2-*O*-(6-Deoxy-α-L-mannopyranosyl)-β-D-glucopyranosyl]oxy]-5-hydroxy-2-(3-hydroxy-4-methoxyphenyl)-2,3-dihydro-4*H*-1-benzopyran-4-one (neohesperidin).

[d] 1-[4-[[2-*O*-(6-Deoxy-α-L-mannopyranosyl)-β-D-glucopyranosyl]oxy]-2,6-dihydroxyphenyl]-3-(4-hydroxyphenyl)propan-1-one (naringin dihydrochalcone).

[e] 1-[4-[[6-*O*-(6-Deoxy-α-L-mannopyranosyl)-β-D-glucopyranosyl]oxy]-2,6-dihydroxyphenyl]-3-(3-hydroxy-4-methoxyphenyl)propan-1-one (hesperidin dihydrochalcone).

[f] 1-[4-(β-D-Glucopyranosyloxy)-2,6-dihydroxyphenyl]-3-(3-hydroxy-4-methoxyphenyl)propan-1-one (hesperetin dihydrochalcone 7'-glucoside).

[g] 3-(3-Hydroxy-4-methoxyphenyl)-1-(2,4,6-trihydroxyphenyl)propan-1-one (hesperetin dihydrochalcone).

SPECIFIC TESTS

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• **Water Determination ⟨921⟩, *Method I*:** NMT 12.0%

• **Microbial Enumeration Tests ⟨61⟩** and **Tests for Specified Microorganisms ⟨62⟩:** The total aerobic microbial count does not exceed 10^3 cfu/g and the total combined molds and yeasts count does not exceed 10^2 cfu/g.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in tight, light-resistant containers.

• **USP Reference Standards ⟨11⟩**

USP Neodiosmin RS

5-Hydroxy-2-(3-hydroxy-4-methoxyphenyl)-4-oxo-4*H*-chromen-7-yl 2-*O*-(α-L-rhamnopyranosyl)-β-D-glucopyranoside.

$C_{28}H_{32}O_{15}$ 608.55

USP Neohesperidin Dihydrochalcone RS

▲ (NF 1-Dec-2019)

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

Topic/Question	Contact	Expert Committee
NEOHESPERIDIN DIHYDROCHALCONE	Documentary Standards Support	SE2020 Simple Excipients

Chromatographic Database Information: Chromatographic Database

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