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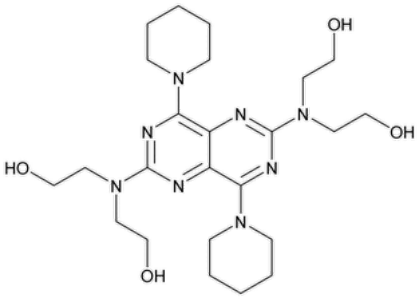
Dipyridamole



$C_{24}H_{40}N_8O_4$ 504.63

Ethanol, 2,2',2",2'"-[(4,8-di-1-piperidinylpyrimido[5,4-*d*]pyrimidine-2,6-diyl)dinitrilo]tetrakis-;

2,2',2",2'"-[(4,8-Dipiperidinopyrimido[5,4-*d*]pyrimidine-2,6-diyl)dinitrilo]tetraethanol CAS RN®: 58-32-2; UNII: 64ALC7F90C.

DEFINITION

Dipyridamole contains NLT 98.0% and NMT 102.0% of dipyridamole ($C_{24}H_{40}N_8O_4$), calculated on the dried basis.

IDENTIFICATION

Change to read:

• **A.** ▲Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: **197K**▲ (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**

Buffer: 0.77 g/L of ammonium acetate. Adjust with glacial acetic acid to a pH of 4.0.

Mobile phase: Methanol and *Buffer* (700:300)

Standard solution: 0.2 mg/mL of USP Dipyridamole RS in methanol

Sample solution: 0.2 mg/mL of Dipyridamole in methanol

Chromatographic system

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

Mode: LC

Detector: UV 288 nm

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

Flow rate: 1.2 mL/min

Injection volume: 10 µL

Run time: NLT 1.7 times the retention time of dipyridamole

System suitability

Sample: *Standard solution*

Suitability requirements

Tailing factor: NMT 1.5

Relative standard deviation: NMT 0.73%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of dipyridamole ($C_{24}H_{40}N_8O_4$) in the portion of Dipyridamole taken:

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

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

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

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

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

Acceptance criteria: 98.0%–102.0% on the dried basis

IMPURITIES

- **Residue on Ignition ⟨281⟩:** NMT 0.1%
- **Organic Impurities**

Solution A: 10 mM ammonium formate. Adjust with formic acid to a pH of 5.0.

Solution B: Acetonitrile

Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0.0	80	20
2.0	80	20
17.0	5	95
19.0	5	95
21.0	80	20
25.0	80	20

Standard solution: 0.5 µg/mL each of USP Dipyridamole RS, USP Dipyridamole Related Compound A RS, USP Dipyridamole Related Compound B RS, USP Dipyridamole Related Compound C RS, USP Dipyridamole Related Compound D RS, USP Dipyridamole Related Compound E RS, and USP Dipyridamole Related Compound F RS in methanol

Sample solution: 500 µg/mL of Dipyridamole in methanol

Chromatographic system

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

Mode: LC

Detector: UV 295 nm

Column: 2.1-mm × 15-cm; 1.7-µm packing L1

Column temperature: 45°

Flow rate: 0.3 mL/min

Injection volume: 2 µL

System suitability

Sample: *Standard solution*

Suitability requirements

Resolution: NLT 4.0 between dipyridamole related compound D and dipyridamole

Relative standard deviation: NMT 2.8%

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of each specified impurity in the portion of Dipyridamole taken:

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

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

r_S = peak response of corresponding USP Reference Standard from the *Standard solution*

C_S = concentration of corresponding USP Reference Standard in the *Standard solution* (µg/mL)

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

Calculate the percentage of each unspecified impurity in the portion of Dipyridamole taken:

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

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

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

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

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

Acceptance criteria: See *Table 2*.

Table 2

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
Dipyridamole related compound B	0.6	0.50
Dipyridamole related compound F	0.7	0.1
Dipyridamole related compound D	0.9	0.2
Dipyridamole	—	—
Dipyridamole related compound E	1.2	0.2
Dipyridamole related compound C	1.5	0.1
Dipyridamole related compound A	1.9	0.50
Any unspecified impurity	—	0.10
Total impurities	—	1.0

SPECIFIC TESTS

- **Chloride**

  Sample: 500 mg

  Analysis: Dissolve the *Sample* in 5 mL of alcohol and 2 mL of 2 N nitric acid. Add 1 mL of silver nitrate TS.

  Acceptance criteria: No turbidity or precipitate is produced.

- **Loss on Drying ⟨731⟩**

  Analysis: Dry at 105° for 3 h.

  Acceptance criteria: NMT 0.2%

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in tight, light-resistant containers. Store at room temperature.
- **USP Reference Standards ⟨11⟩**

USP Dipyridamole RS

USP Dipyridamole Related Compound A RS

2,2'-{[4,6,8-Tri(piperidin-1-yl)pyrimido[5,4-*d*]pyrimidin-2-yl]azanediyl}diethanol.

$C_{25}H_{40}N_8O_2$ 484.64

USP Dipyridamole Related Compound B RS

2,2',2",2‴,2⁗,2⁗'-{[8-(Piperidin-1-yl)pyrimido[5,4-*d*]pyrimidine-2,4,6-triyl]tris(azanetriyl)}hexaethanol.

$C_{23}H_{40}N_8O_6$ 524.61

USP Dipyridamole Related Compound C RS

2,2'-{[6-Chloro-4,8-di(piperidin-1-yl)pyrimido[5,4-*d*]pyrimidin-2-yl]azanediyl}diethanol.

$C_{20}H_{30}ClN_7O_2$ 435.95

USP Dipyridamole Related Compound D RS

2,2'-({6-[(2-Hydroxyethyl)amino]-4,8-di(piperidin-1-yl)pyrimido[5,4-*d*]pyrimidin-2-yl}azanediyl)diethanol.

$C_{22}H_{36}N_8O_3$ 460.57

USP Dipyridamole Related Compound E RS

2,2',2",2‴-{[6,8-Di(piperidin-1-yl)pyrimido[5,4-*d*]pyrimidine-2,4-diyl]bis(azanetriyl)}tetraethanol.

$C_{24}H_{40}N_8O_4$ 504.63

USP Dipyridamole Related Compound F RS

2,2',2",2‴-({4-[(2-Hydroxyethyl)amino]-8-(piperidin-1-yl)pyrimido[5,4-*d*]pyrimidine-2,6-diyl}bis(azanetriyl))tetraethanol.

$C_{21}H_{36}N_8O_5$ 480.56

Topic/Question	Contact	Expert Committee
DIPYRIDAMOLE	Documentary Standards Support	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

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