NMIA D750b: Papaverine hydrochloride

Report ID: D750b.2025.01 (Bottled 180629)

Chemical Formula: C20H21NO4.HCl

Molecular Weight: 375.8 g/mol (HCl), 339.4 g/mol (base)

# Certified value

|  |  |  |
| --- | --- | --- |
| **Batch No.** | **CAS No.** | **Purity (mass fraction)** |
| **17-D-07** | **61-25-6 (HCl)****58-74-2 (base)** | **99.5 ± 0.5%** |

The uncertainty has been calculated according to ISO Guide 35 and is stated at the 95% confidence limit (k = 2).

IUPAC name 1-(3,4-Dimethoxybenzyl)-6,7-dimethoxyisoquinoline hydrochloride

Expiration of certification: The property values are valid till 24 June 2033, eight years from the date of re-certification provided the **unopened** material is handled and stored in accordance with the recommendations below. The material as issued in the unopened container and stored as recommended below should be suitable for use beyond this date, subject to confirmation of batch stability from the issuing body. The expiry date/shelf life does not apply to sample bottles that have been opened. In such cases, it is recommended that the end-user conduct their own in-house stability trials.

**Description:** Off-white powder sourced from an external supplier, certified for identity and purity by NMI Australia. Packaged in amber glass bottles with a septum and crimped aluminium cap or screw top cap.

Intended use: This certified reference material is suitable for use as a primary calibrator.

**Instructions for use:** Equilibrate the bottled material to room temperature before opening.

Recommended storage: When not in use this material should be stored at or below 25 ºC in a closed container in a dry, dark area.

Metrological traceability: The certified purity value is traceable to the SI unit for mass (kg) through Australian national standards via balance calibration. In the mass balance approach all impurities are quantified as a mass fraction and subtracted from 100%. Quantitative NMR provides an independent direct measure of the mass fraction of the analyte of interest, calibrated with an internal standard certified for purity (mass fraction).

**Stability:** This material has demonstrated stability over a minimum period of five years. The measurement uncertainty at the 95% confidence interval includes a stability component which has been estimated from annual and accelerated stability trials.

The long-term stability of the compound in solution has not been examined.

Homogeneity assessment: The homogeneity of the material was assessed using purity assay by GC-FID on ten randomly selected 1-2 mg sub samples of the material. The material was judged to be sufficiently homogeneous at this level of sampling as the variation in analysis results between samples was not significantly different at a 95% confidence level from that observed on repeat analysis of the same sample.

Safety: Treat as hazardous substance. Use appropriate work practices when handling to avoid skin or eye contact, ingestion or inhalation of dust. Refer to the provided safety data sheet.



Dr Stephen R. Davies,

Team Leader,

Chemical Reference Materials, NMI.

9 July 2025

This report supersedes any issued prior to 9 July 2025.

NATA Accreditation No. 198 / Corporate Site No. 14214.

**CIPM MRA notice:** This certificate is consistent with the capabilities that are included in Appendix C of the CIPM MRA drawn up by the CIPM. Under the CIPM MRA, all participating institutes recognize the validity of each other’s calibration and measurement certificates for the quantities, ranges and measurement uncertainties specified in Appendix C. The “CIPM MRA Logo” and this statement attest only to the measurement(s) applied for determining the certified values on the certificate (for details see <http://www.bipm.org>).

**Legal notice:** Terms and Conditions associated with the provision of this reference material can be found on the NMIA website.

Characterisation Report:

The purity value was obtained from a combination of traditional analytical techniques and quantitative nuclear magnetic resonance (qNMR). The techniques used in the mass balance approach include GC-FID, thermogravimetric analysis, Karl Fischer analysis and 1H NMR spectroscopy. The purity value is calculated as per Equation 1.

Purity = (100 % - IORG) x (100 % - IVOL – INVR) Equation 1

IORG = Organic impurities of related structure, IVOL = volatile impurities, INVR = non-volatile residue.

The purity value by qNMR was obtained using a combination of the one-proton singlets at 7.3 and 7.4 ppm, the one-proton doublet at 7.9 ppm and the one-proton doublet at 8.1 ppm measured against a certified internal standard of dimethyl sulfone.

Supporting evidence is provided by qualitative headspace GC-MS analysis of occluded solvents and elemental microanalysis.

GC-FID: Instrument: Agilent 6890 or 8890

 Column: HP-1, 30 m × 0.32 mm I.D. × 0.25 m

 Program: 200 °C (0.5 min), 6 °C/min to 280 °C (1 min), 20 °C /min to 300 °C (3 min)

 Injector: 250 °C

 Detector Temp: 320 °C

 Carrier: Helium

 Split ratio: 20/1

 Relative mass fraction of main component:

 Initial analysis: Mean = 100%, s = 0.02% (10 sub samples in duplicate, July 2017)

 Re-analysis: Mean = 100%, s = 0.01% (5 sub samples in duplicate, July 2018)

 Re-analysis: Mean = 100%, s = 0.01% (5 sub samples in duplicate, June 2021)

 Re-analysis: Mean = 99.95%, s = 0.003% (5 sub samples in duplicate, June 2025)

Thermogravimetric analysis: Volatile content, 0.1% and non volatile residue < 0.2% mass fraction (June 2016)

Karl Fischer analysis: Moisture content ≤ 0.2% mass fraction (July 2017, June 2018, April 2021 & July 2025)

 Moisture content 0.13% mass fraction (June 2018)

QNMR: Instrument: Bruker Avance-III-500

 Field strength: 500 MHz

 Solvent: D2O (4.79 ppm)

 Internal standard: Dimethyl sulfone (100% mass fraction)

 Initial analysis: Mean (7.3 & 7.4 ppm) = 99.6%, s = 0.3% (5 sub samples, November 2017)

 Initial analysis: Mean (7.9 ppm) = 99.5%, s = 0.4% (5 sub samples, November 2017)

 Initial analysis: Mean (8.1 ppm) = 99.8%, s = 0.2% (5 sub samples, November 2017)

**Spectroscopic and other characterisation data**

ESI-MS: Instrument: Micromass Quatro LC Micro

 Operation: Positive ion mode, direct infusion at 10 L/min

 Ionisation: ESI spray voltage at 3.2 kV positive ion

 EM voltage: 650 V

 Cone voltage: 45 V

 Peak: 340.2 (M+H+) *m/z*

GC-MS: Instrument: Agilent 6890/5973

 Column: HP-1MS, 30 m x 0.25 mm I.D. x 0.25 m

 Program: 180 C (1 min), 15 C/min to 300 C (3 min)

 Injector: 250 C

 Transfer line temp: 280 C

 Carrier: Helium, 1.0 mL/min

 Split ratio: 20/1

The retention time of the free base is reported along with the major peaks in the mass spectrum. The latter are reported as mass/charge ratios and (in brackets) as a percentage relative to the base peak.

 Free base (10.7 min): 339 (M+, 74), 338 (100), 324 (89), 308 (22), 293 (11), 281 (11), 207 (19), 154 (13) *m/z*

HS-GC-MS: Instrument: Agilent 6890/5973/G1888

 Column: DB-624, 30 m x 0.25 mm I.D. x 1.4 m

 Program: 50 C (5 min), 7 C/min to 120 C, 15 °C/min to 220 °C (8.3 min)

 Injector: 150 C

 Transfer line temp: 280 C

 Carrier: Helium, 1.2 mL/min

 Split ratio: 50/1

 Solvents detected: Toluene, acetone

TLC: Conditions: Kieselgel 60F254. Methanol / 33% aqueous ammonia (200/3)

 Single spot observed, Rf = 0.8. Visualisation with UV at 254 nm

IR: Instrument: Biorad FTS300MX FT-IR

 Range: 4000-400 cm-1, KBr powder

 Peaks: 2500, 1994, 1955, 1635, 1608, 1508, 1436, 1409, 1282, 1146 cm-1

1H NMR: Instrument: Bruker Avance III 500

 Field strength: 500 MHz

 Solvent: D2O (4.79 ppm)

 Spectral data: 3.63 (3H, s), 3.70 (3H, s), 3.84 (3H, s) 3.87 (3H, s), 6.72 (1H, dd, *J* = 1.8, 8.3 Hz), 6.79 (1H, d, *J* = 8.3 Hz), 6.91 (1H, d, *J* = 1.7 Hz), 7.21 (1H, s), 7.35 (1H, s), 7.82 (1H, d, *J* = 6.5 Hz), 8.10 (1H, d, *J* = 6.5 Hz) ppm

 Acetone estimated at 0.03% mass fraction was observed in the 1H NMR.

13C NMR: Instrument: Bruker Avance III 500

 Field strength: 126 MHz

 Solvent: D2O

 Spectral data:  36.6, 55.6, 55.7, 56.3, 56.6, 104.6, 106.4, 112.1, 112.3, 121.7, 122.1, 122.2, 127.9, 129.5, 137.1, 147.8, 148.7, 151.9, 154.0, 156.4 ppm

Melting point: 221.0-225.2 C

Microanalysis: Found: C = 63.7%; H = 5.9%; N = 3.8%, Cl = 9.4% (August 2017)

 Calculated: C = 63.9%; H = 5.9%; N = 3.7%, Cl = 9.4% (Calculated for C20H21NO4.HCl)

**Amendment record**

Original report ID: D750b.2017.01 (GT/SRD)

Date of issue: 28 September 2017

Date of revision: 4 July 2018

Revised report ID: D750b.2018.01 (Bottled 180629)

Revisions:

* Report ID updated to show the bottling date

Date of revision: 24 July 2018 (MK/MM)

Revised report ID: D750b.2018.01 (Bottled 180629)

Revisions:

* Routine stability trial and purity statement updated to 99.8 ± 1.9 % as the previous report was showing incorrect value of 99.9 ± 0.9%

Date of revision: 20 February 2020 (MK/SRD)

Revised report ID: D750b.2018.02 (Bottled 180629)

Revisions:

* Insert CAS of free base
* Insert IUPAC name
* Update the report into new template

Date of revision: 25 June 25, 2021 (YL/MM)

Revised report ID: D750b.2021.01 (Bottled 180629)

Revisions:

* Routine stability trial
* Government logo updated and side number updated
* Stability comment error fixed and updated
* . purity statement updated to 99.8 ± 0.9 %

Date of revision: 15 September 2022 (TD)

Revised report ID: D750b.2021.02 (Bottled 180629)

Revisions:

* Update to the new template (change departmental name, NATA logo…)

Date of revision: 7 July 2025 (JH/SRD)

Revised report ID: D750b.2025.01 (Bottled 180629)

Revisions:

* Routine stability (GC-FID & KF) – no change