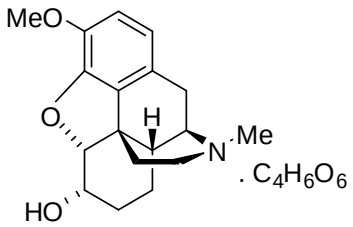
Australian Government
Department of Industry, Science and Resources

National Measurement Institute

NATA
WORLD RECOGNISED ACCREDITATION

CERTIFIED REFERENCE MATERIAL CERTIFICATE OF ANALYSIS

NMIA D823: Dihydrocodeine hydrogen tartrate



Report ID: D823.2022.02

Chemical Formula: $C_{18}H_{23}NO_3.C_4H_6O_6$

Molecular Weight: 451.5 g/mol (tartrate), 301.4 g/mol (base)

Certified value

Batch No.	CAS No.	Purity (mass fraction)
03-D-11	**5965-13-9 (tartrate)** **125-28-0 (base)**	**98.9% ± 0.6%**

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

IUPAC name: (2R,3R)-2,3-Dihydroxysuccinic acid - (5α,6α)-3-methoxy-17-methyl-4,5-epoxymorphinan-6-ol

Expiration of certification: The property values are valid till 30 March 2027, i.e. five 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 NMIA. 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% coverage interval includes a stability component which has been estimated from annual 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.

Caution: Treat as a 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.

S. R. Davies

Dr Stephen R. Davies,
Team Leader,
Chemical Reference Materials, NMI.
15 September 2022

This report supersedes any issued prior to 15 September 2022.

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

Characterisation Report:

The identity was confirmed by a range of spectroscopic techniques, NMR, IR and MS. The certified purity value was obtained by mass balance from a combination of traditional analytical techniques, including GC-FID, thermogravimetric analysis, Karl Fischer analysis and ^{1}H NMR spectroscopy. The purity value is calculated as per Equation 1.

Purity = (100 % - I_{ORG}) x (100 % - I_{VOL} – I_{NVR}) Equation 1

I_{ORG} = Organic impurities of related structure, I_{VOL} = volatile impurities, I_{NVR} = non-volatile residue.

Supporting evidence is provided by elemental microanalysis.

GC-FID:	Instrument:	Agilent 6890A / Agilent 8890
	Column:	HP-1, 30 m x 0.32 mm I.D. x 0.25 μm
	Program	180 °C (1 min), 8 °C/min to 230 °C (4 min), 30 °C/min to 300 °C (3 min)
	Injector:	250 °C
	Detector Temp:	320 °C
	Carrier:	Helium
	Split ratio:	20/1
	Relative mass fraction of the main component as the free base:	
	Initial analysis:	Mean = 99.2%, s = 0.84% (10 sub samples in duplicate, August 2003)
	Re-analysis:	Mean = 99.2%, s = 0.01% (5 sub samples in duplicate, February 2010)
	Re-analysis:	Mean = 99.3%, s = 0.03% (5 sub samples in duplicate, December 2012)
	Re-analysis:	Mean = 99.2%, s = 0.03% (5 sub samples in duplicate, October 2017)
	Re-analysis:	Mean = 99.2%, s = 0.05% (5 sub samples in duplicate, April 2022)
Thermogravimetric analysis:		Volatiles content < 0.1% and non-volatile residue < 0.2% mass fraction (September 2003 & November 2005)
Karl Fischer analysis:		Moisture content < 0.5% mass fraction (January & February 2010, December 2012, October 2017 and April 2022)

Spectroscopic and other characterisation data

GC-MS:	Instrument:	HP6890/5973
	Column:	Zebron ZB-5, 30 m x 0.25 mm I.D. x 0.30 μm
	Program:	130 °C (1 min), 15 °C/min to 320 °C (5 min)
	Injector:	250 °C
	Transfer line temp:	280 °C
	Carrier:	Helium, 1.0 mL/min
	Split ratio:	30/1
	The retention time of the free base is reported with the major peaks in the mass spectrum. The latter are reported in mass/charge ratios and (in brackets) as a percentage relative to the base peak.	
	Free base (11.5 min):	301 (M^+, 100), 286 (12), 284 (14), 244 (16), 185 (10), 164 (20), 70 (12) *m/z*
TLC:	Conditions:	Kieselgel 60F_{254}. Diisopropylether/diethylether/diethylamine (45/45/10) Single spot observed, R_f = 0.7 (3 samples)
IR:	Instrument:	Biorad FTS 3000MX FT-IR
	Range:	4000-400 cm^{-1}, KBr
	Peaks:	3469, 2931, 1615, 1508, 1443, 1275, 1192, 1123, 1072, 934, 902 cm^{-1}
^{1}H NMR:	Instrument:	Bruker DMX500
	Field strength:	500 MHz
	Solvent:	MeOH-D4 (3.35 ppm)
	Key spectral data:	δ 2.69 (3H,s), 3.25 (1H,d, J = 19.5 Hz), 3.92 (3H,s), 4.08 (1H,dd, J = 5.1, 10.0 Hz), 4.48 (2H,s), 4.68 (1H,d, *J* = 5.1 Hz), 6.76 (1H, d, J = 8.3 Hz), 6.89 (1H, d, J =8.3 Hz) ppm
^{13}C NMR:	Instrument:	Bruker DMX600
	Field strength:	150.9 MHz
	Solvent:	D_2O
	Spectral data:	δ 17.9, 20. 7, 26.5, 34.5, 39.1, 40.1, 40.4, 41.1, 48.1, 56.9, 62.0, 66.4, 89.5, 115.4, 120.3, 124.2, 128.5, 141. 9, 146.4, 176.7 ppm
Melting point:		186-189 °C
Microanalysis:	Found:	C = 58.5%; H = 6.5%; N = 3.1% (September 2003)
	Calculated:	C = 58.5%; H = 6.5%; N = 3.1% (Calc. for $C_{18}H_{23}NO_3.C_4H_6O_6$)