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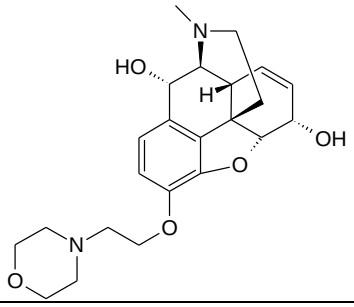
# Reference Material Product Information Sheet

Epichem's Quality System conforms to ISO9001:2015 as certified by ECAAS Pty Ltd - Certification number 616061.




| | |
|---|---|
| **Name** | 10-hydroxypholcodine |
| **Synonym(s)** | (5α,6α,10α)-7,8-didehydro-4,5-epoxy-17-methyl-3-(2-(4-morpholinyl)ethoxy)-morphinan-6,10-diol |
| **Epichem Item #** | EPL-AA89 Batch 12 |
| **CAS #** | 433308-87-3 |
| **Molecular Formula** | $C_{23}H_{30}N_2O_5$ |
| **Molecular Weight** | 414.51 g/mol |
| **Appearance** | Yellow powder |
| **Melting Point** | 56.0-94.6°C (decomposition). |
| **Combustion Analysis** | Required (%): C:66.6; H:7.3; N:6.8. Found (%): C:64.6; H:7.5; N:6.6. |
| **Purity*** | 96.5% |
| **Date of Manufacture** | 23 July 2020 |
| **Storage Requirements** | Hygroscopic. Protect from heat, light and moisture. |
| **Special Precautions** | **This compound is for laboratory use only. Its toxicological properties may not have been fully established. It should be handled only by suitably qualified personnel.** |
| **Intended Use** | This compound is suitable for the identification of impurities and degradants in pharmaceutical materials. The purity assay is considered as relative contribution. |
| **Date of Shipment** | TBA<br>This certificate is valid for one year from the date of shipment provided the substance is stored under the recommended conditions. |
| **Retest Date** | TBA (Proper Storage and Handling Required) |

** NATA accreditation does not cover the performance of this service*





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## I. Identity

The identity of this product was established using the following analyses:

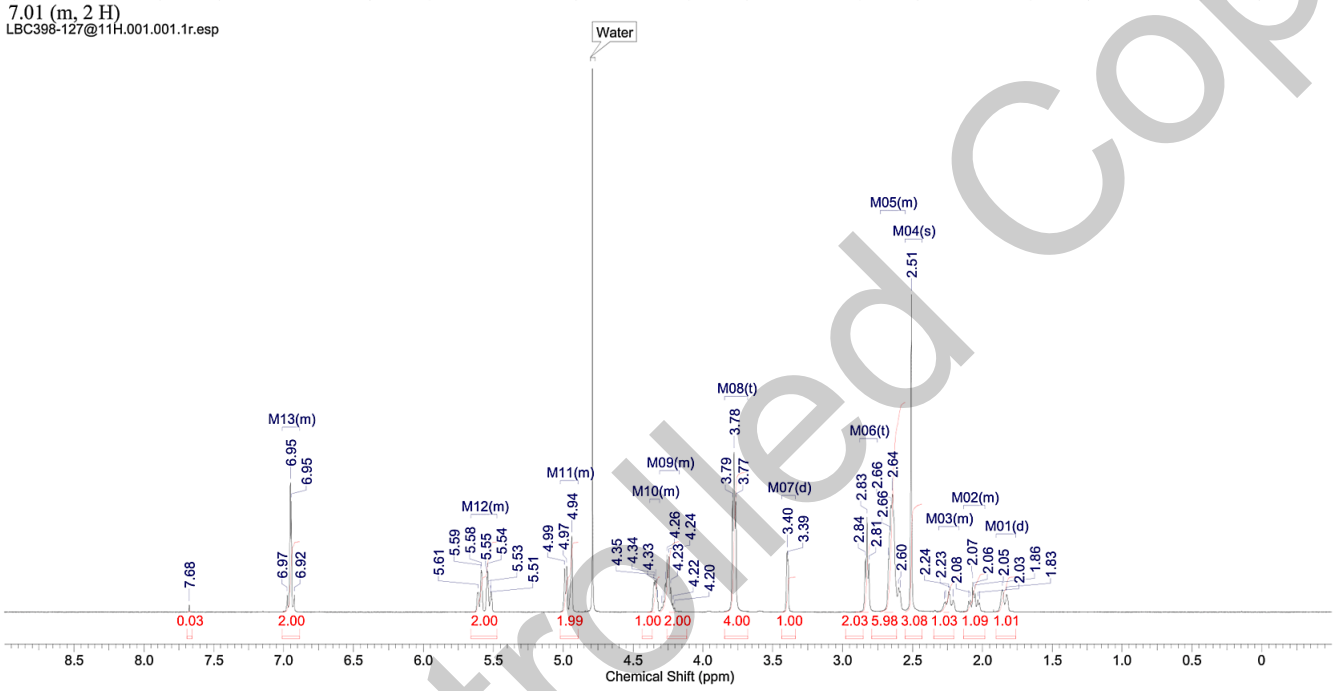
### Ia. $^{1}$HNMR Spectrum

Conditions: 400 MHz, $D_2O$

$^{1}$HNMR spectrum consistent with chemical structure.

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| *Acquisition Time (sec)* | 3.7547 | *Comment* | LBC398-127@11H 1H D2O {E:\dataexternal\epichem} cygoh 8 | | | *Date* | 23 Jul 2020 17:40:16 |
| *Date Stamp* | 23 Jul 2020 17:40:16 | | | *File Name* | \\NAPHTHALENE\Company\NMR files\LBC398-127@11H\1\pdata\1\1r | | |
| *Frequency (MHz)* | 400.13 | *Nucleus* | 1H | *Number of Transients* | 8 | *Origin* | spect |
| *Original Points Count* | 24038 | *Owner* | nmr | *Points Count* | 32768 | *Pulse Sequence* | zg |
| *Receiver Gain* | 128.00 | *SW(cyclical) (Hz)* | 6402.05 | *Solvent* | DEUTERIUM OXIDE | | |
| *Spectrum Offset (Hz)* | 2835.7646 | *Spectrum Type* | STANDARD | *Sweep Width (Hz)* | 6401.85 | *Temperature (degree C)* | 24.996 |

$^{1}$H NMR (400 MHz, DEUTERIUM OXIDE) δ ppm 1.84 (d, *J*=12.70 Hz, 1 H) 1.98 - 2.14 (m, 1 H) 2.17 - 2.31 (m, 1 H) 2.51 (s, 3 H) 2.55 - 2.73 (m, 6 H) 2.83 (t, *J*=5.28 Hz, 2 H) 3.39 (d, *J*=2.54 Hz, 1 H) 3.78 (t, *J*=4.69 Hz, 4 H) 4.17 - 4.31 (m, 2 H) 4.31 - 4.38 (m, 1 H) 4.89 - 5.02 (m, 2 H) 5.47 - 5.66 (m, 2 H) 6.88 - 7.01 (m, 2 H)





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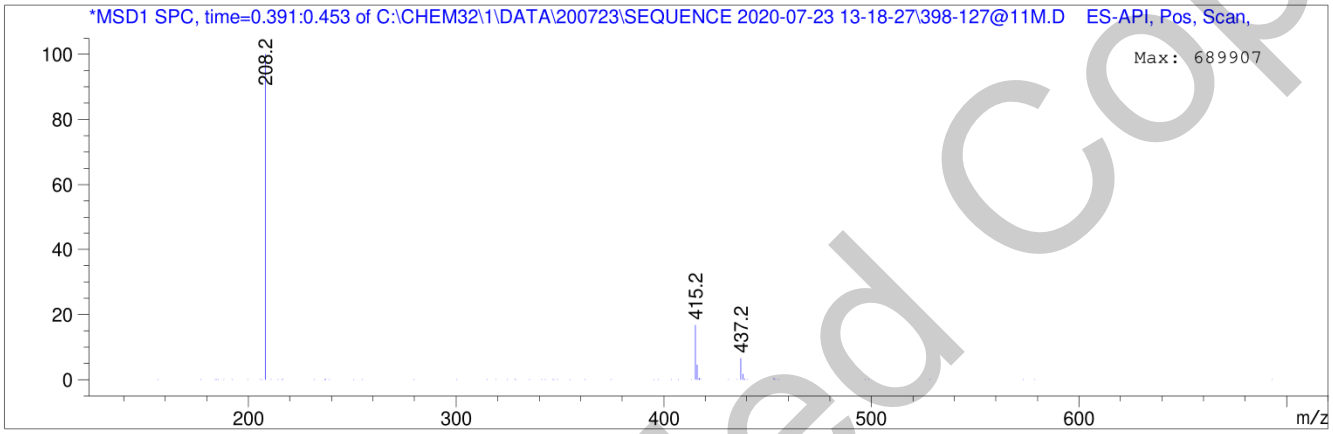
## Ib. Mass Spectrum

The mass spectrum of this material was analysed by Liquid Chromatography Mass Spectroscopy (LCMS) using in-house EM005.WI08.

Method: ACN/water gradient (+ 0.1% formic acid).

ZORBAX SB-C8, 4.6 x 30 mm, 3.5 micron.

| Retention Time (MS) | MS Area | Mol. Weight or Ion |
|---|---|---|
| 0.418 | 5936462 | 415.20 I<br>208.20 I |




Theoretical value: 415.2 $[M+H]^+$.

The signal of the Mass Spectrum is consistent with the theoretical value and its interpretation is consistent with the structural formula.





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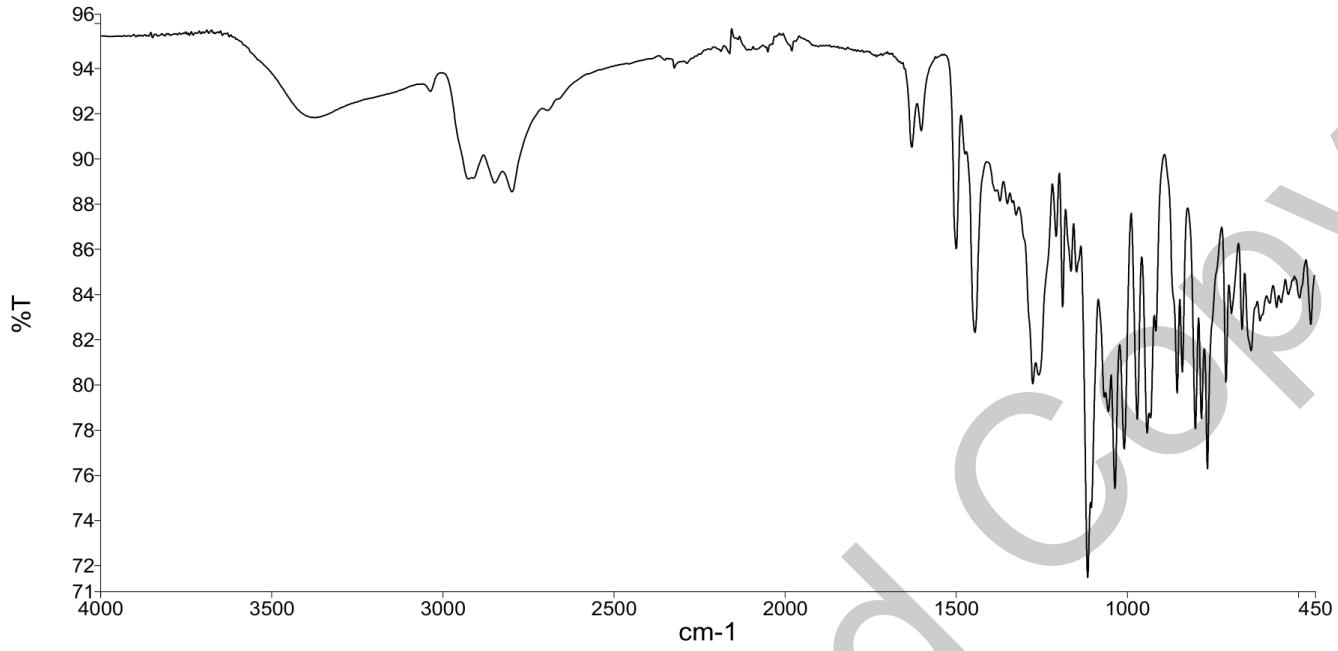
## Ic. IR Spectrum

The infra-red spectrum of this material was analysed by Fourier-Transform Infrared Spectroscopy (FTIR) using in-house EM005.WI09.




The interpretation of the signals of the Fourier-Transform Infrared Spectrum is consistent with the structural formula.





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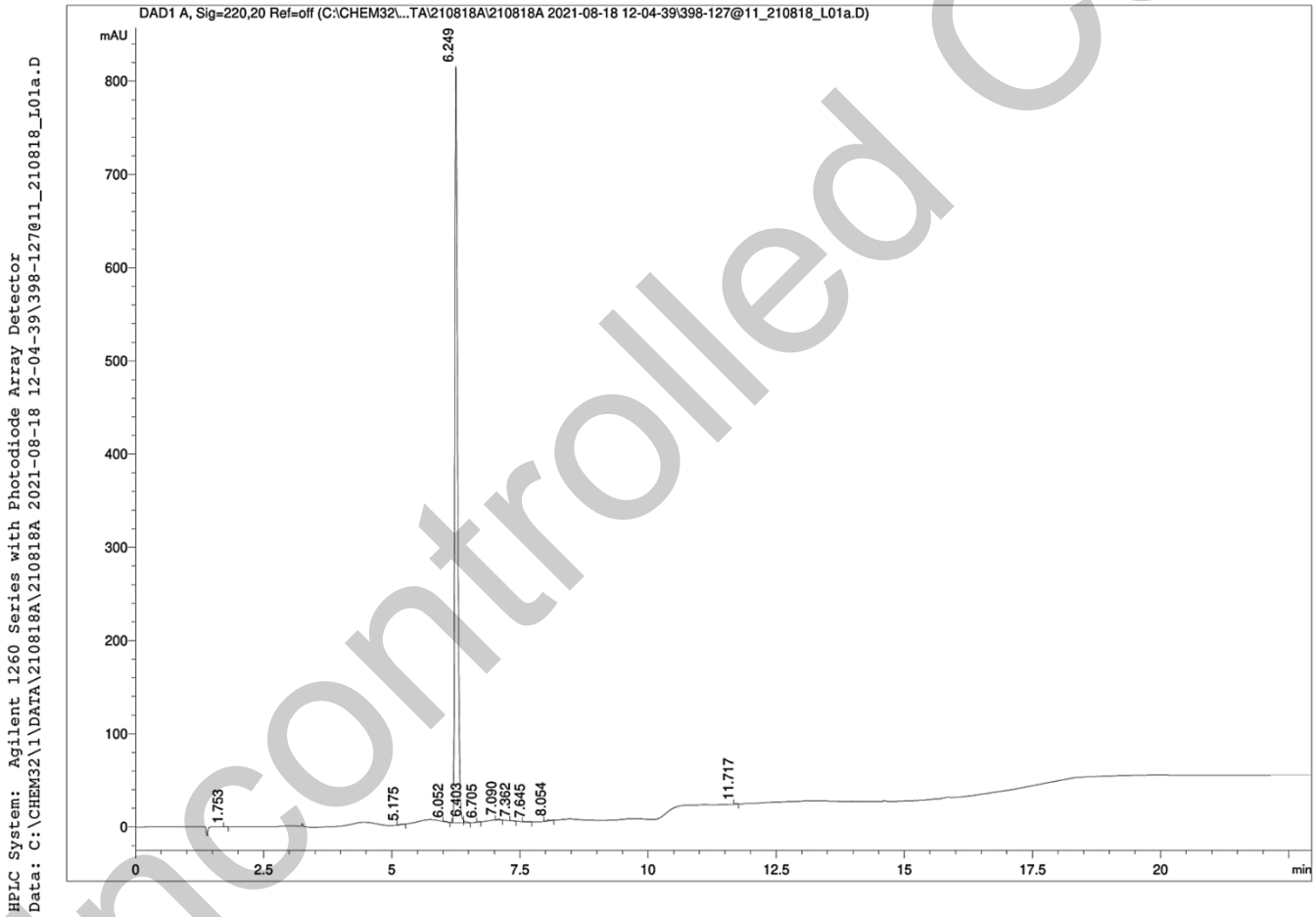
## II. Purity

The purity of this material was analysed by high performance liquid chromatography (HPLC) using in-house EM005.WI07.

## HPLC Conditions:

| Column | Conditions | | | | Detector | Injector |
|---|---|---|---|---|---|---|
| Fortis H2o<br><br>4.6 x 100mm<br><br>3 micron | 25ºC | | | | DAD<br><br>220nm | Auto<br><br>1.0 µL<br><br>1.4 mg/mL in 100% water (NO MODIFIERS) |
| | Time (min) | % Line A (Water + 0.1% (v/v) TFA) | % Line B (Acetonitrile + 0.1% (v/v) TFA) | Flow rate (mL/min) | | |
| | 0.00 | 99.5 | 0.5 | 1.0 | | |
| | 8.00 | 87.5 | 12.5 | 1.0 | | |
| | 16.25 | 5 | 95 | 1.0 | | |
| | 21.25 | 5 | 95 | 1.0 | | |
| | 22.25 | 99.5 | 0.5 | 1.0 | | |
| | 28.25 | 99.5 | 0.5 | 1.0 | | |





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**Area Percent Report – Sorted by Signal**

| Peak Number | Retention Time (rounded) | Area | Area % (rounded) |
|---|---|---|---|
| 1 | 1.75 | 0.24 | 0.01 |
| 2 | 5.18 | 1.06 | 0.04 |
| 3 | 6.05 | 1.74 | 0.06 |
| 4 | 6.25 | 3000.40 | 99.21 |
| 5 | 6.40 | 7.76 | 0.26 |
| 6 | 6.70 | 0.61 | 0.02 |
| 7 | 7.09 | 4.05 | 0.13 |
| 8 | 7.36 | 1.23 | 0.04 |
| 9 | 7.64 | 1.20 | 0.04 |
| 10 | 8.05 | 4.34 | 0.14 |
| 11 | 11.72 | 1.53 | 0.05 |
| Totals | | | 100 (rounded) |

For the calculation the system peaks were ignored. The content of the analyte was determined as a ratio of the peak area of the analyte and the cumulative areas of the purities, added up to 100%.

**Results:**

Average 99.2% (average of 10 duplicate runs)





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## III. Water Content

Method: Karl-Fischer titration using in-house EM005.WI04.
**Results:**
Average 1.8%

## IV. Ash Content

Method: BP 2016 Ash (Appendix XI J) as per WS001/28614
**Result:**
Contains <0.1% ash.

## V. Residual Solvents

Method: $^{1}$HNMR
**Result:**
0.9% chloroform detected by $^{1}$H NMR analysis.

## VI. Final Result

| | |
|---|---|
| Chromatographic purity (HPLC) | 99.2% |
| Water content | 1.8% |
| Ash content | <0.1% |
| Residual solvents | 0.9% |
| Purity* | 96.5% |

This purity is assessed to be 96.5%.

Product Reviewed By:

James Rixson, PhD
Head of Production

Product Released By:

Carol Worth, PhD
Quality Manager
Release Date: 21 September 2021

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**NATA accreditation does not cover the performance of this service.*
The calculation of the purity follows the formula:

$$\text{Purity}(\%) = \frac{((\text{Chromatographicpurity[HPLC]})x(100 - (\text{watercontent} + \text{ashcontent} + \text{volatilecontents})))}{100}$$





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