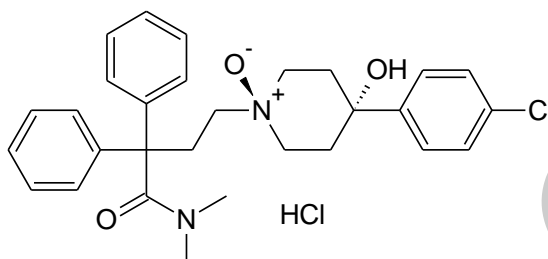


Reference Material Product Information Sheet

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



Name	4-[<i>trans</i> -4-(4-chlorophenyl)-4-hydroxy-1-oxidopiperidin-1-yl]- <i>N,N</i> -dimethyl-2,2-diphenylbutanamide hydrochloride
BP/EP Name	Loperamide Impurity F
USP Name	Loperamide Related Compound F
Synonym(s)	<i>trans</i> -Loperamide- <i>N</i> -oxide hydrochloride, Loperamide oxide hydrochloride, <i>trans</i> -4-(4-chlorophenyl)-4-hydroxy- <i>N,N</i> -dimethyl- α,α -diphenyl-1-piperidinebutanamide 1-oxide
Epichem Item #	EPL-AA56 Batch 1
CAS #	2575516-34-4
Molecular Formula	C ₂₉ H ₃₃ ClN ₂ O ₃ .HCl
Molecular Weight	529.51 g/mol
Appearance	Pale yellow powder
Melting Point	105.4-140.0°C (decomposition)
Combustion Analysis	Required (%): C:65.8; H:6.5; N:5.3. Found (%): C:64.8; H:6.6; N:4.9.
Purity*	94.5%
Date of Manufacture	23 November 2009
Storage Requirements	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 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

EPL-AA56 Batch 1

Revision 4

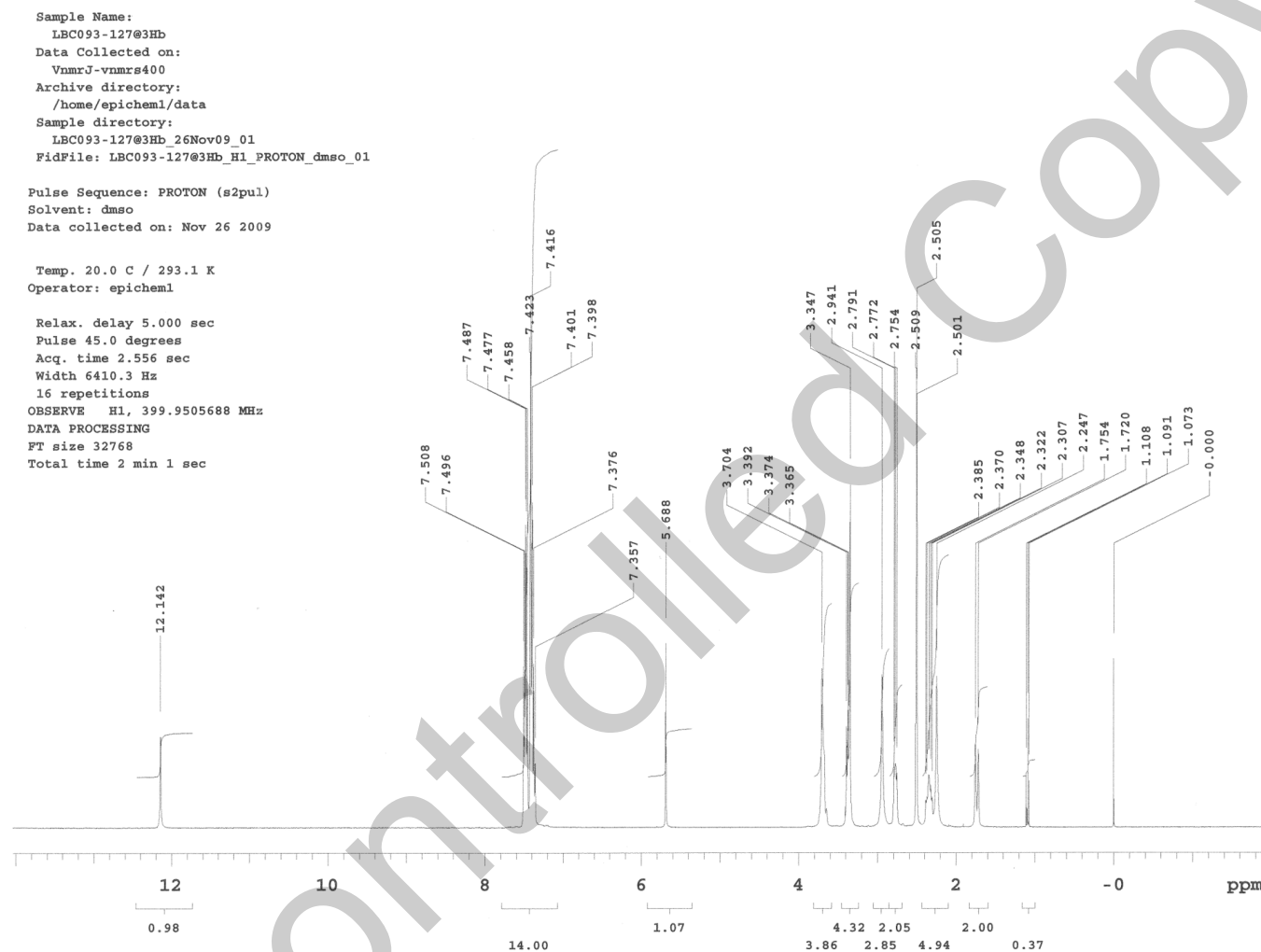
Epichem Pty Ltd, Suite 5, 3 Brodie-Hall Drive, Bentley WA 6102, Australia
Tel + 61 (0)8 6167 5200 Fax + 61 (0)8 6167 5201 www.epichem.com.au ABN 80 106 769 902

I. Identity

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

Ia. ¹HNMR Spectrum

Conditions: 400 MHz, DMSO-d₆
¹HNMR spectrum consistent with chemical structure.



EPL-AA56 Batch 1

Revision 4

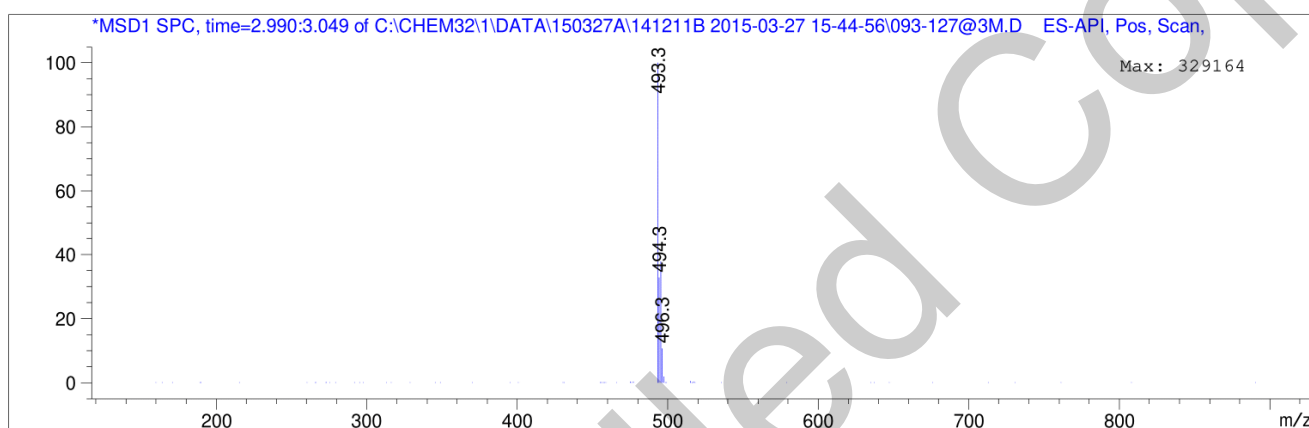
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Ib. Mass Spectrum

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

Method: 5% to 100% ACN in water gradient (+0.1% formic acid)
Poroshell 120 EC-C18, 4.6 x 50 mm, 2.7 micron

Retention Time (MS)	MS Area	Mol. Weight or Ion
3.016	3774256	496.30 495.30 494.30 493.30



Theoretical value: 494.3 [M+H]⁺.

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

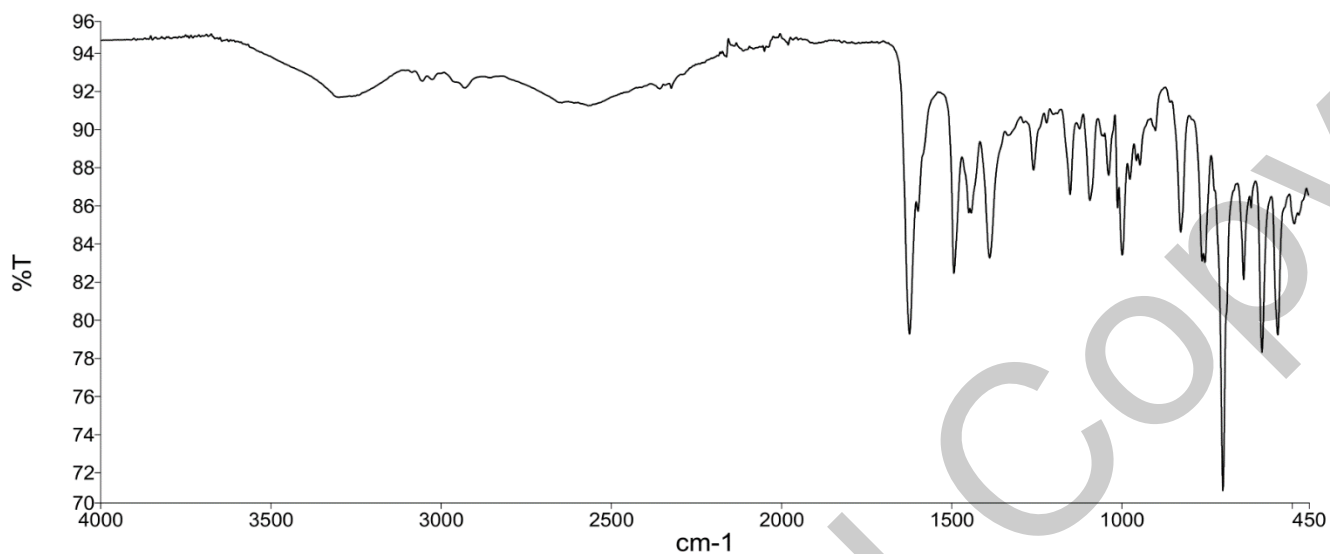
EPL-AA56 Batch 1

Revision 4

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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.

EPL-AA56 Batch 1

Revision 4

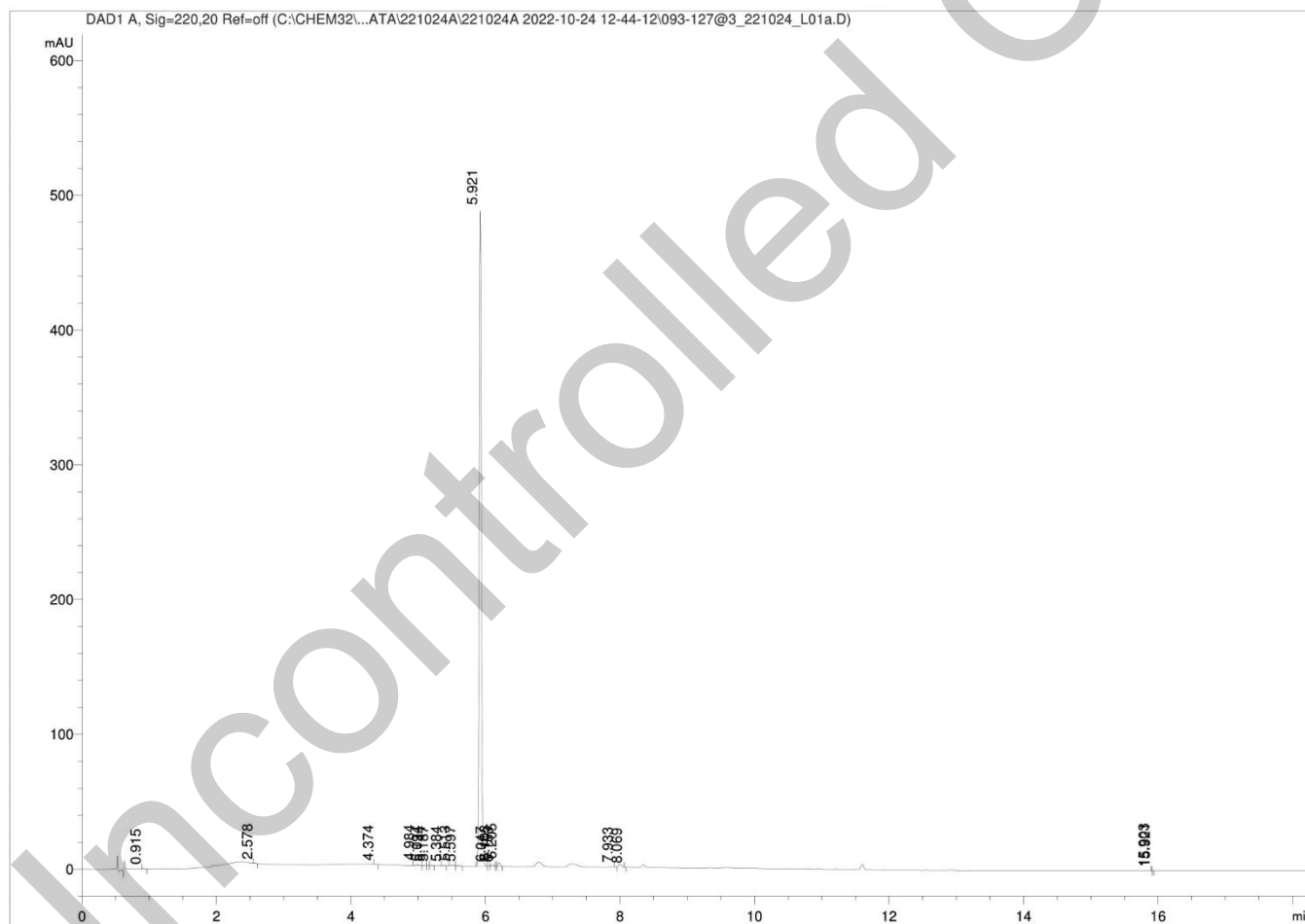
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II. Purity

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

HPLC Conditions:

Column	Conditions				Detector	Injector
Agilent Poroshell 120 EC-C18 4.6 x 50mm 2.7 micron	25°C				DAD 220nm	Auto 1.0 µL 0.5 mg/mL in 100% methanol (NO MODIFIERS)
	Time (min)	% Line A (5 mM tetrabutylammonium bisulfate in water)	% Line B (acetonitrile, no modifiers)	Flow rate (mL/min)		
	0.00	86	14	1.0		
	8.00	46	54	1.0		
	12.10	5	95	1.0		
	17.10	5	95	1.0		
	18.10	86	14	1.0		
	23.10	86	14	1.0		



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Area Percent Report – Sorted by Signal

Peak Number	Retention Time (rounded)	Area	Area % (rounded)
1	0.91	0.84	0.08
2	2.58	0.30	0.03
3	4.37	0.06	0.01
4	4.98	2.38	0.23
5	5.09	0.24	0.02
6	5.14	0.53	0.05
7	5.19	0.73	0.07
8	5.38	0.31	0.03
9	5.51	1.51	0.14
10	5.60	0.74	0.07
11	5.92	1040.31	98.37
12	6.05	0.59	0.06
13	6.10	3.03	0.29
14	6.15	0.28	0.03
15	6.20	5.20	0.49
16	7.93	0.15	0.01
17	8.07	0.05	0.00
18	15.90	0.05	0.00
19	15.92	0.21	0.02
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 98.3% (average of 10 duplicate runs)

III. Water Content

Method: Karl-Fischer titration using in-house EM005.WI04.

Results:

Average 2.7%

IV. Ash Content

Method: Combustion adjuvant added

Result:

Contains 0.3% ash.

V. Residual Solvents

Method: ¹H NMR

Result:

0.9% Diethyl Ether by ¹H NMR analysis.

VI. Final Result

Chromatographic purity (HPLC)	98.3%
Water content	2.7%
Ash content	0.3%
Residual solvents	0.9%
Purity*	94.5%

This purity is assessed to be 94.5%.

Product Reviewed By:

Product Released By:

James Rixson, PhD
Head of Production

Carol Worth, PhD
Quality Manager
Release Date: 28 October 2022

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

The calculation of the purity follows the formula:

$$\text{Purity(\%)} = \frac{((\text{Chromatographic purity[HPLC]}) \times (100 - (\text{water content} + \text{ash content} + \text{volatile contents})))}{100}$$

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