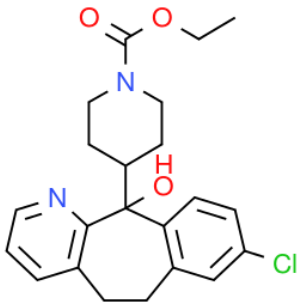
Our Formula. Your Success.

Reference Material Product Information Sheet

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



Name	Ethyl 4-(8-chloro-6,11-dihydro-11-hydroxy-5H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl)-1-piperidinecarboxylate
BP/EP Name	Loratadine Impurity A
USP Name	Hydroxyloratadine
Synonym(s)	Ethyl 4-(8-chloro-11-hydroxy-5,6-dihydro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-yl) piperidin-1-carboxylate; 11-Hydroxy dihydro loratadine
Epichem Item #	EPL-AA278 Batch 1
CAS #	133284-74-9
Molecular Formula	$C_{22}H_{25}ClN_2O_3$
Molecular Weight	400.91 g/mol
Appearance	White solid
Melting Point	121.6-127.9°C
Combustion Analysis	Required (%): C:65.9; H:6.3; N:7.0. Found (%): C:66.3; H:6.3; N:7.0.
Purity*	99.6%
Date of Manufacture	15 March 2021
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 unopened and 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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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:

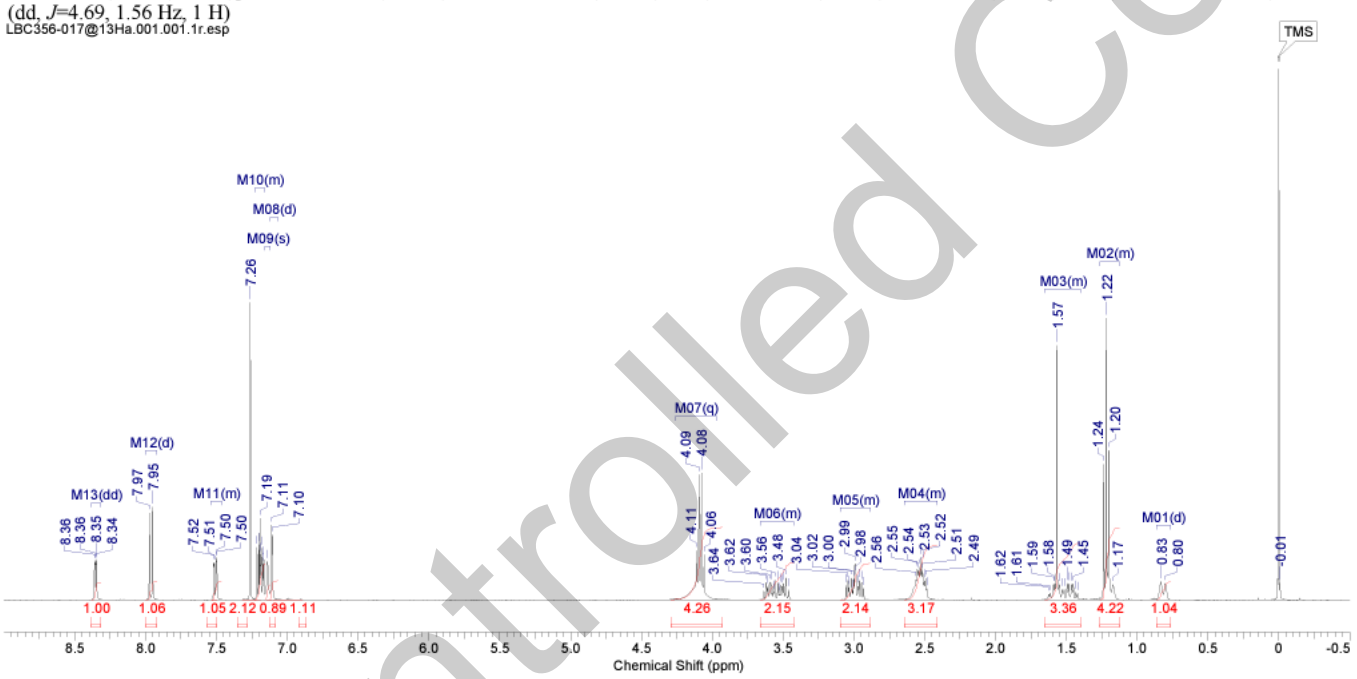
Ia. ^{1}HNMR Spectrum

Conditions: 400 MHz, $CDCl_3$

^{1}H NMR spectrum consistent with chemical structure.

Acquisition Time (sec)	3.7547	***Comment***	LBC356-017@13Ha 1H CDCl3 {E:\dataexternal\epichem} cygoh 13				
Date	12 Oct 2020 17:12:32			***Date Stamp***	12 Oct 2020 17:12:32		
File Name	\\naphthalene\company\NMR files\LBC356-017@13Ha\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***	161.00
SW(cyclical) (Hz)	6402.05	***Solvent***	CHLOROFORM-d			***Spectrum Offset (Hz)***	2791.1384
Spectrum Type	STANDARD	***Sweep Width (Hz)***	6401.85	***Temperature (degree C)***	25.104		

^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 0.82 (d, *J*=13.09 Hz, 1 H) 1.13 - 1.26 (m, 4 H) 1.40 - 1.65 (m, 3 H) 2.41 - 2.64 (m, 3 H) 2.89 - 3.09 (m, 2 H) 3.43 - 3.66 (m, 2 H) 4.08 (q, *J*=7.10 Hz, 4 H) 7.11 (d, *J*=2.34 Hz, 1 H) 7.14 (s, 1 H) 7.16 - 7.23 (m, 2 H) 7.47 - 7.54 (m, 1 H) 7.96 (d, *J*=8.60 Hz, 1 H) 8.35 (dd, *J*=4.69, 1.56 Hz, 1 H)



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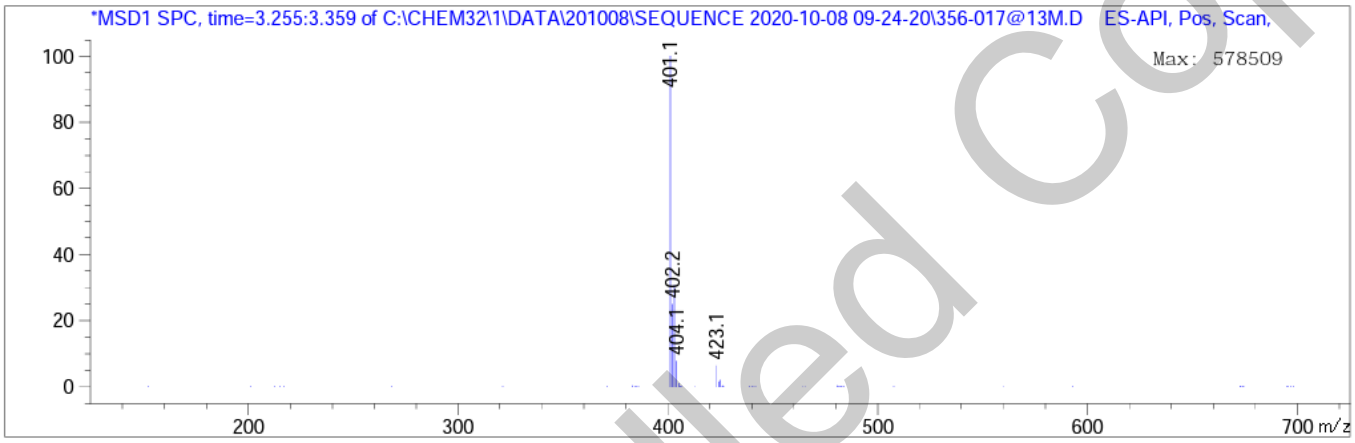
Ib. Mass Spectrum

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
3.296	10005111	403.10 I
		402.20 I
		401.15 I



Theoretical value: 401.1 [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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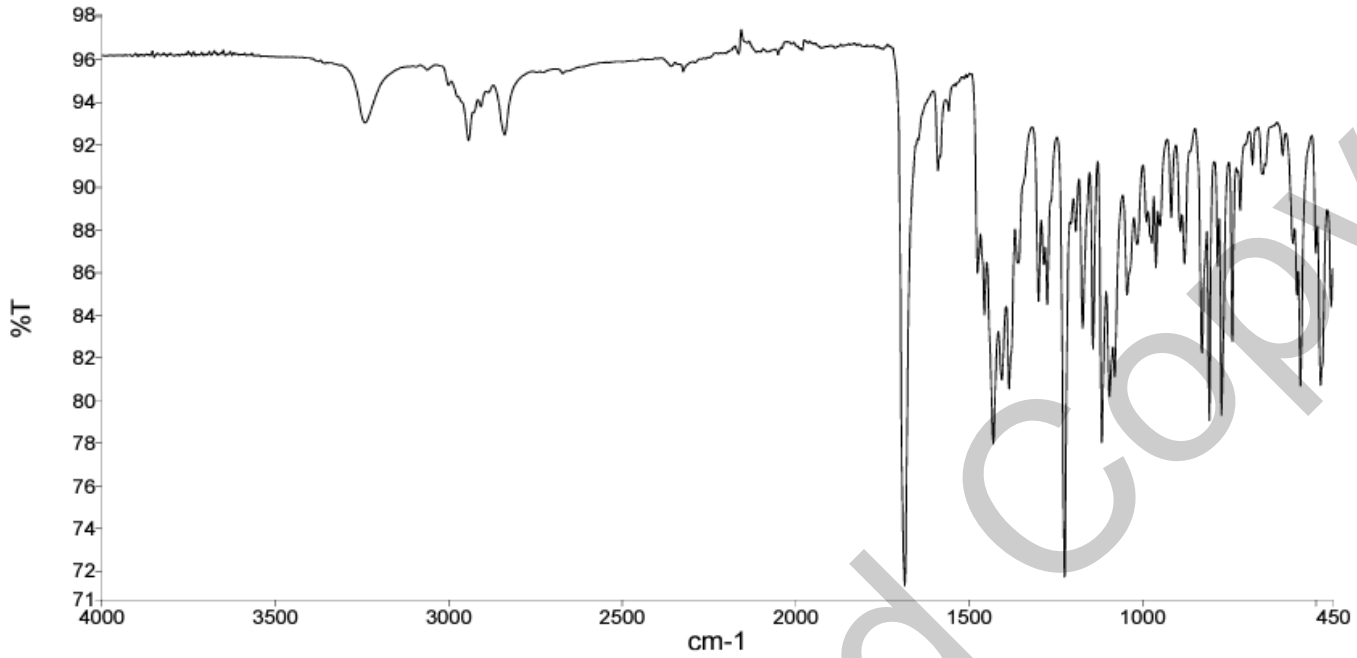
Ic. IR Spectrum

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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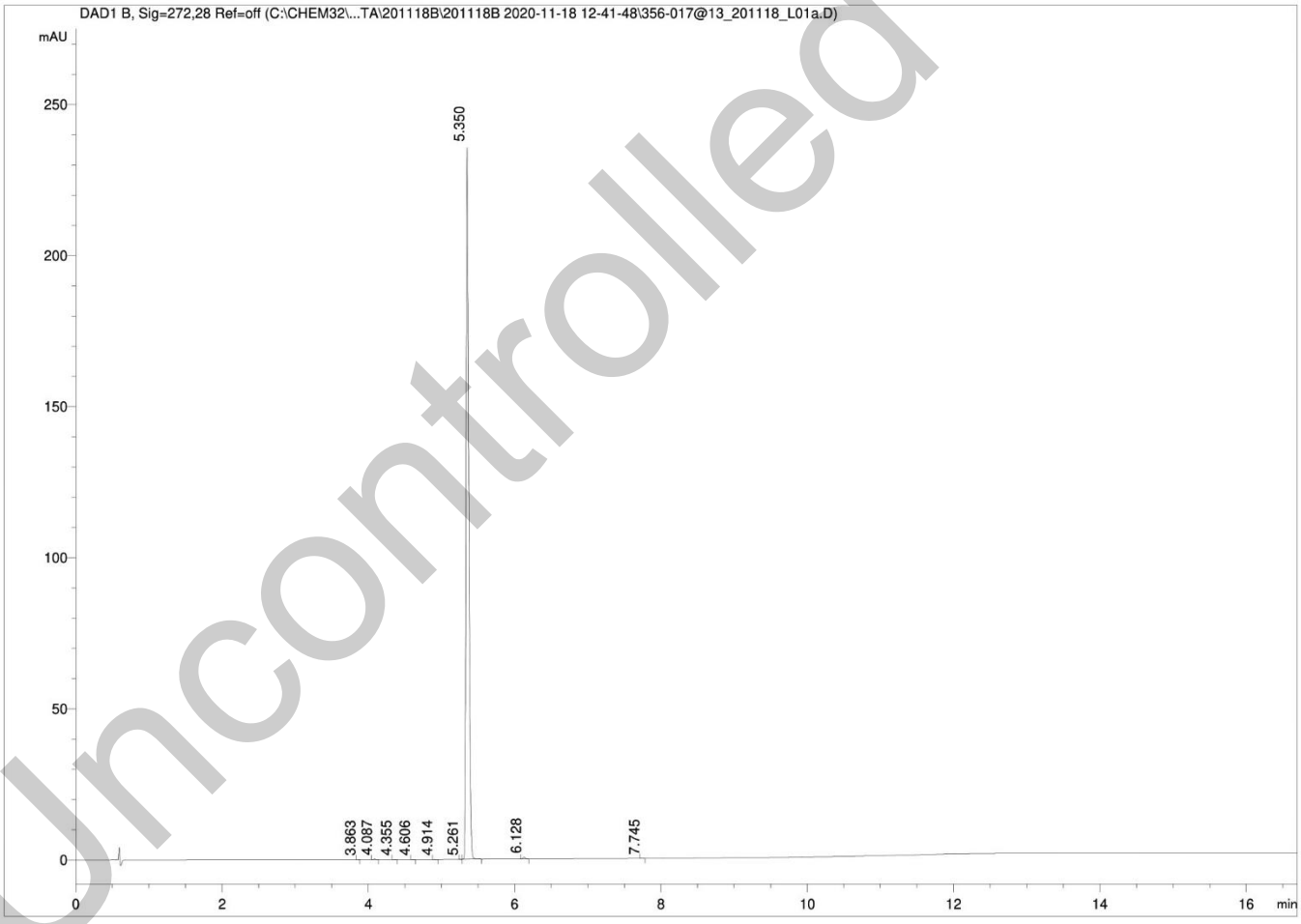
II. Purity

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

HPLC Conditions:

Column	Conditions				Detector	Injector
Agilent Poroshell 120 EC-C18 4.6 x 50mm 2.7 micron	25ºC				DAD 272nm	Auto 1.0 µL 0.6 mg/mL in 100% acetonitrile (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	80	20	1.0		
	6.00	50	50	1.0		
	10.50	5	95	1.0		
	15.50	5	95	1.0		
	16.50	80	20	1.0		
	19.50	80	20	1.0		



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Area Percent Report – Sorted by Signal

Peak Number	Retention Time (rounded)	Area	Area % (rounded)
1	3.86	0.02	0.00
2	4.09	0.33	0.05
3	4.35	0.03	0.01
4	4.61	0.06	0.01
5	4.91	0.03	0.01
6	5.26	0.03	0.00
7	5.35	603.37	99.66
8	6.13	1.49	0.25
9	7.74	0.05	0.01
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 99.7% (average of 10 duplicate analyses)

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III. Water Content

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

Results:

Average 0.1%

IV. Ash Content

Method: BP2020 Ash Appendix XI J Method II

Result:

Contains <0.1% ash.

V. Residual Solvents

Method: ^{1}HNMR

Result:

No significant impurities detected by ^{1}H NMR analysis.

VI. Final Result

Chromatographic purity (HPLC)	99.7%
Water content	0.1%
Ash content	<0.1%
Residual solvents	<0.1%
Purity*	99.6%

This purity is assessed to be 99.6%.

Product Reviewed By:

James Rixson, PhD
Head of Production

Product Released By:

Carol Worth, PhD
Quality Manager

Release Date: 22 July 2022

**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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