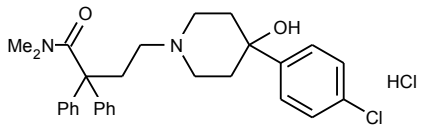
BDG SYNTHESIS

Certificate of Analysis

BDG Synthesis certifies that this reference material meets or exceeds the specifications stated herein.

Neil Beare, PhD, Director
2 July 2016

Name:	**Loperamide HCl**
CAS Number:	34552-83-5
Structure:	
Molecular Weight:	$C_{29}H_{33}ClN_2O_2 \cdot HCl = 513.50$
Lot Number:	BDG 4646
Appearance:	White, crystalline powder
Corrected Purity:	99.5 % (HPLC) - 0.2 % (2-propanol) - 0.3 % (water) = 99.0 %
Re-test Date:	2 July 2021

Storage and Handling:

Temperature:	refrigerate for prolonged storage; may be handled and shipped at ambient temperature.
Humidity:	not believed to be hygroscopic; may be handled in normal laboratory atmosphere.
Light:	protect from strong sunlight.
Caution:	only experienced laboratory personnel should handle the material.

• Analytical reference standards, metabolites, stable isotope labelled compounds • Custom synthesis • FTE contract research

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Identity and Purity

Proton NMR Spectrum

Identity: the signals are consistent with the proposed structure and in accord with literature where available.
Residual Solvents: a small amount of 2-propanol (0.2 % *w/w*) is observed.
Impurities: traces of unidentified impurities are seen in the baseline.

Carbon-13 NMR Spectrum

Identity: the signals are consistent with the proposed structure and in accord with literature where available.

High-resolution Mass Spectrum (ESI+)

Found *m/z* 477.2290. $C_{29}H_{34}{}^{35}ClN_2O_2$ $[M+H]^+$ requires *m/z* 477.2303. The deviation of 2.9 ppm is within normally accepted limits for the establishment of identity by HRMS.

HPLC

A sharp, symmetrical peak is observed (99.5 %). Note: in the absence of reference materials for preparing calibration curves, it is assumed that all peaks have the same detector response. Where possible, the conditions of analysis follow a pharmacopeial or literature method, or have been adapted from same.

Elemental Analysis

	Found:	C 67.18, H 6.79, N 5.41 %
$C_{29}H_{33}ClN_2O_2 \cdot HCl \cdot 0.3H_2O$	Requires:	C 67.12, H 6.72, N 5.40 %
$C_{29}H_{33}ClN_2O_2 \cdot HCl$	Requires:	C 67.83, H 6.67, N 5.46 %

The elemental analyses fall slightly outside those expected for anhydrous material; the presence of water is reasonably expected from the method of purification and/or the type of material, and the “best-fit” hydrated molecular formula is given.

Karl-Fischer Analysis

	Found:	H_2O 0.3 %
$C_{29}H_{33}ClN_2O_2 \cdot HCl \cdot 0.3H_2O$	Requires:	H_2O 1.0 %

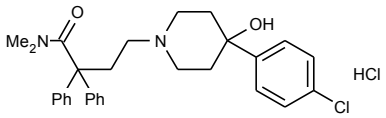
Of necessity, only a small sample could be used and only a single or duplicate analysis performed. We are unable to state what the errors in the reported water content are, but recommend that the result be used, as the best available, when determining corrected purity.

The available quantity of custom-synthesised material is always small, and this limits the extent and type of analytical data which can be obtained. This Certificate is presented in descriptive format for use by analytical chemists who are trained in the use of custom-synthesised materials. Custom materials often contain higher levels of residual solvents and/or water, and we urge you to use the corrected purity where needed rather than the raw HPLC purity. This compound is intended for use as an analytical reference material and it is not for human administration. Structures are shown with relative stereochemistry unless otherwise specified.

The re-test date is assigned from experience gained with the material in the laboratory and/or on storage. It is not possible to perform formal storage studies because of the small amount of material available.

BDG SYNTHESIS

Proton NMR Spectrum of Loperamide HCl in DMSO-d_6



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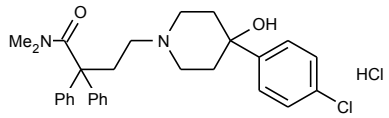
BDG SYNTHESIS

Carbon-13 NMR Spectrum of Loperamide HCl in DMSO-d_6



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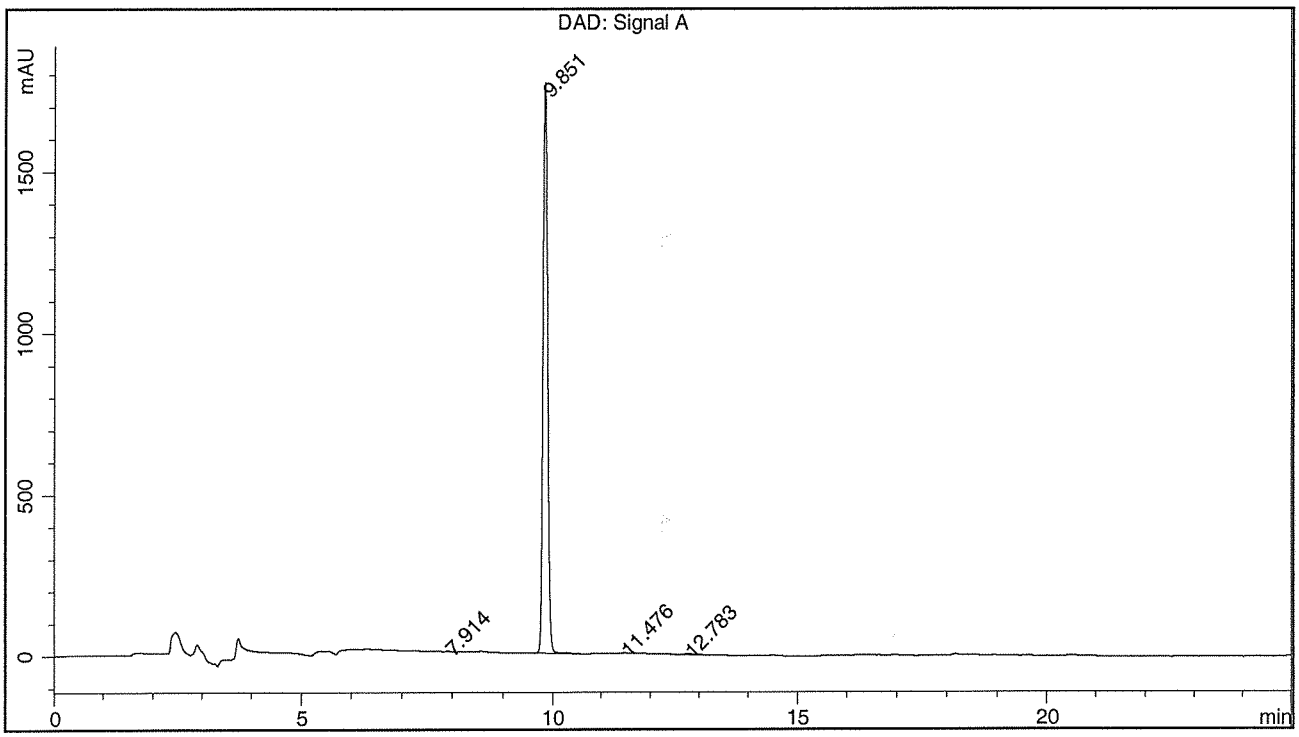
BDG - Analysis of Loperamide HCl

Column : Phenomenex Luna C18(2) 5um 250 x 4.6 mm
Guard : Phenomenex Security Guard C18 RP 4 x 3 mm
Mobile Phase A : 75:25 25 mM Tetrabutylammonium Hydroxide pH=2.0 (H2SO4)
Mobile Phase B : 30:70 25 mM Tetrabutylammonium Hydroxide pH=2.0 (H2SO4) : Acetonitrile
Gradient (A:B) : T0=100:0, T15=0:100, T29=0:100, T31=100:0, T35=100:0
Flow Rate : 1.0 mL/min
Sample Solvent : Methanol
Column Temperature : 35 C
Injection Volume : 10 uL
Detection : UV at 220 nm

Sample Name	BDG 4646	Instrument	AnalyticalLC01
Acquisition	02/07/2016, 17:34:22	Method (rev.)	LC10386b (8)
Sequence	BDG_02Jul2016b - Reprocessed	Vial Position	22
Operator	solvation010\cerityadmin	Injection	1 of 1



Area Percent Report

Peak#	RT	Peak Height	Peak Area	Width	Area %
1	7.91 min	1.5070	8.1511	0.0811 min	0.073 %
2	9.85 min	1768.5324	11155.2092	0.0996 min	99.476 %
3	11.48 min	2.3297	15.5753	0.1020 min	0.139 %
4	12.78 min	1.7670	35.0391	0.2373 min	0.312 %