BDG SYNTHESIS

Certificate of Analysis

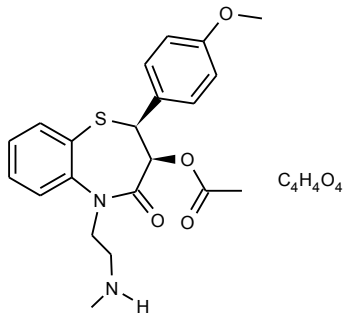
BDG Synthesis certifies that this reference material meets or exceeds the specifications stated herein.

Neil Beare, PhD, Director
15 April 2016

Name: ***N*-Desmethyldiltiazem Maleate**

CAS Number: 86408-45-9 (free base)

Structure:



Molecular Weight: $C_{21}H_{24}N_2O_4S{\cdot}C_4H_4O_4$ = 516.56

Lot Number: BDG 4765.2

Appearance: White, crystalline solid

Purity By HPLC: 98.1 %

Re-test Date: 15 April 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.

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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. The complexity of the spectrum indicates that two rotamers of the product are present in solution.
Residual Solvents: no residual solvents are observed.
Impurities: no significant impurities are evident in the spectrum.

Carbon-13 NMR Spectrum

Identity: the signals are consistent with the proposed structure and in accord with literature where available. Most signals are duplicated indicating that two rotamers of the product are present in solution.

High-resolution Mass Spectrum (ESI+)

Found *m/z* 401.1535. $C_{21}H_{25}N_2O_4S$ $[M+H]^+$ (free base) requires *m/z* 401.1530. The deviation of 1.2 ppm is within normally accepted limits for the establishment of identity by HRMS.

HPLC

A broad, slightly tailing peak is observed (98.1 %). The peak on the solvent front is from maleic acid, confirmed by a spiking experiment. 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 58.29, H 5.47, N 5.54 %
$C_{21}H_{24}N_2O_4S{\cdot}C_4H_4O_4$	Requires:	C 58.13, H 5.46, N 5.42 %

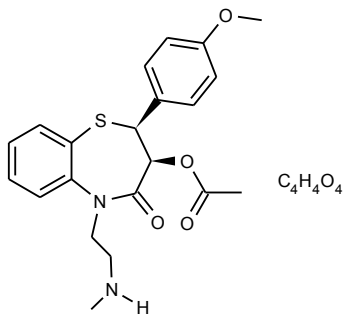
The elemental analyses fall within generally accepted limits for establishing the molecular formula given. The results may also be taken to imply the absence of significant quantities of water or inorganic salts (which have not been elsewhere tested for because of sample size limitations).

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

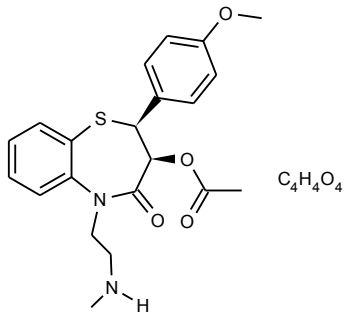
Proton NMR Spectrum of *N*-Desmethyldiltiazem Maleate in DMSO-d_6



Lot Number: BDG 4765.2

BDG SYNTHESIS

Carbon-13 NMR Spectrum of *N*-Desmethyldiltiazem Maleate in DMSO-d_6

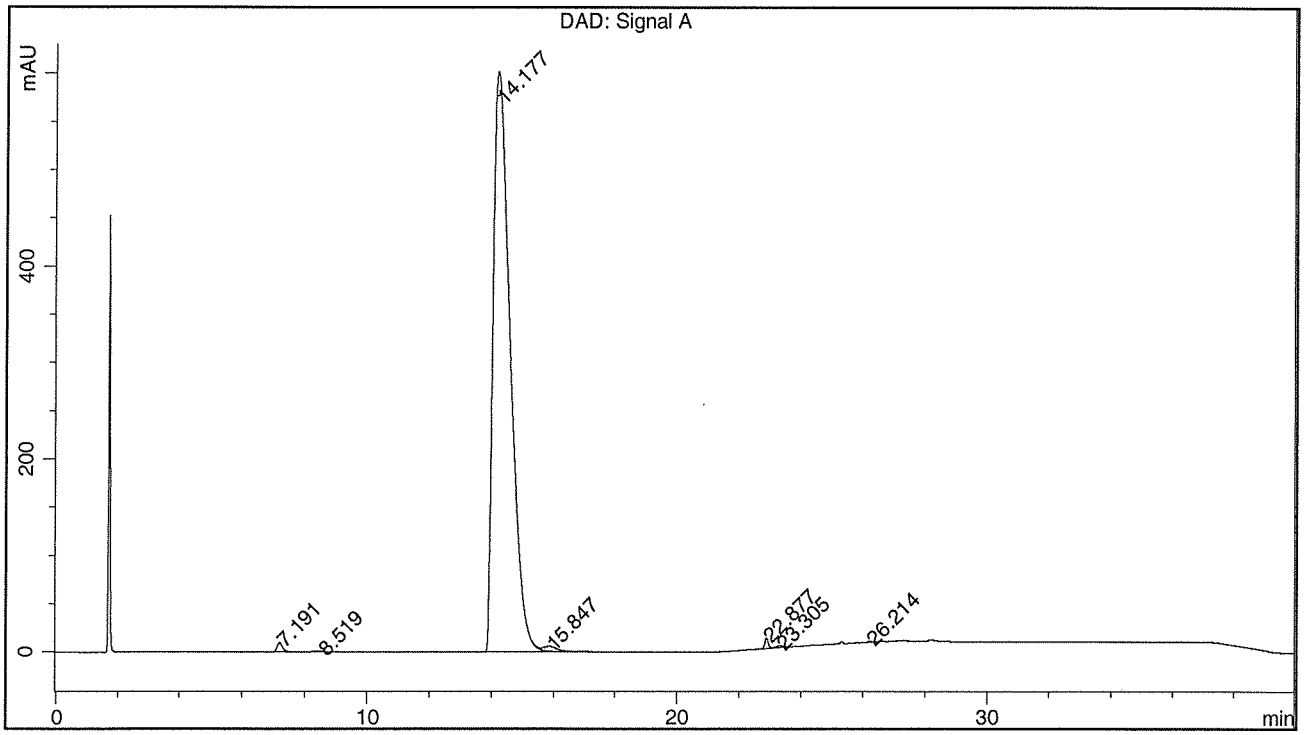


Lot Number: BDG 4765.2

BDG - Analysis of N-Desmethyldiltiazem Maleate

Column : Phenomenex Luna C18(2) 5um 250 x 4.6 mm
Guard : Phenomenex Security Guard C18 RP 4 x 3 mm
Mobile Phase A : 70:25:5 50mM KH2PO4 + 0.02% Triethylamine pH=4.5 (H3PO4) : Acetonitrile : Ethanol
Mobile Phase B : Acetonitrile
Gradient (A:B) : T0=100:0, T18=100:0, T25=50:50, T35=50:50, T36=100:0, T40=100:0
Flow Rate : 1.5 mL/min
Sample Solvent : 70:30 Water : Acetonitrile
Column Temperature : 20 C
Injection Volume : 10 uL
Detection : UV at 240 nm

Sample Name	BDG 4765.2	Instrument	AnalyticalLC01
Acquisition	15/04/2016, 18:51:10	Method (rev.)	LC10355c (14)
Sequence	BDG_15Apr2016c - Reprocessed	Vial Position	3
Operator	solvation010\cerityadmin	Injection	1 of 2



Area Percent Report

Peak#	RT	Peak Height	Peak Area	Width	Area %
1	7.19 min	10.1009	125.9054	0.1894 min	0.537 %
2	8.52 min	0.9676	24.1851	0.3396 min	0.103 %
3	14.18 min	601.8858	22991.1848	0.5757 min	98.115 %
4	15.85 min	5.2657	179.7381	0.4882 min	0.767 %
5	22.88 min	10.9310	83.5075	0.1171 min	0.356 %
6	23.31 min	1.6009	22.7194	0.2236 min	0.097 %
7	26.21 min	1.0250	5.6788	0.0846 min	0.024 %