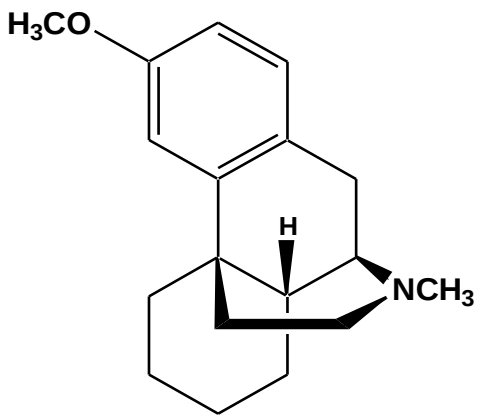
DEXTROMETHORPHAN

Latest Revision: June 23, 2005



1. SYNONYMS

CFR: Not controlled (OTC)

CAS #: 125-71-3
Hydrobromide anhydrous: 125-69-9
Hydrobromide monohydrate: 6700-34-1

Other Names: (+)-3-Methoxy-17-methylmorphinan
Dextromethorphan hydrobromide
Demorphan hydrobromide
Ro-1-5470/5
Benylin DM
Canfodion
Cosylan
Hihustan
M

2. CHEMICAL AND PHYSICAL DATA

2.1. CHEMICAL DATA

Form	Chemical Formula	Molecular Weight	Melting Point (°C)
Base	$C_{18}H_{25}NO$	271.4	109-113
Hydrobromide	$C_{18}H_{25}NO \cdot HBr \cdot H_20$	370.3	125

2.2. SOLUBILITY

Form	C	E	W

Hydrobromide	fs	vss	ps
Base	fs		Vss

C = chloroform, E = ether and W = water, VS = very soluble, FS = freely soluble, S = soluble, PS = sparingly soluble, SS = slightly soluble, VSS = very slightly soluble and I = insoluble

3. SCREENING TECHNIQUES

3.1. COLOR TESTS

REAGENT	COLOR PRODUCED
Liebermann's	Black
Froehde[1]	Blue-green

3.2. CRYSTAL TESTS

REAGENT	CRYSTALS PRODUCED
PbI_2-KOAc	Bunches of serrated plates[1]
H_2PtCl_6	Feathery rosettes[1]

3.3. THIN LAYER CHROMATOGRAPHY

Visualization

Acidified Iodoplatinate Purple/violet

COMPOUND	Relative Rf Values		
	System TLC5	System TLC18	System TLC6
Dextromethorphan	1.0	1.0	1.0
Hydrocodone	0.73	0.09	1.1
Methadone	1.4	1.3	1.1
Morphine	1.08	0.0	0.5

3.4. GAS CHROMATOGRAPHY

Method DXM- GCS1

Internal Standard Stock Solution (ISSS):
0.05 mg/mL tetracosane in chloroform:methanol (4:1).

Standard Solution Preparation:
Accurately weigh and prepare standard solutions at approximately 0.05 mg/mL using the above internal standard stock solution.

Sample Preparation:
Weigh approximately 20 mg into a GC vial (~2mL). Fill with ISSS. If necessary, filter sample through glass wool.

Instrument: Agilent 6890 Series II (or comparable) gas chromatograph operated in split mode equipped with a FID detector

Column: 5% Phenyl/95% Methyl silicone gum 12 m x 0.2 mm x 0.33 µm film thickness

Carrier gas: Helium at 1.0 mL/min for 5 min ramped flow to 2.0 mL/min

Temperatures: Injector: 270°C
Detector: 280°C
Oven program:
1) 175°C initial temperature for 1.0 min
2) Ramp to 280°C at 15°C/min
3) Hold final temperature for 4.0 min

Injection Parameters: Split Ratio = 60:1, 1 µL injection

Typical Retention Time: Dextromethorphan: 5.18 min
Tetracosane : 5.97 min

COMPOUND	RRT	COMPOUND	RRT
dimethylsulfone	0.114	propoxyphene HCl	1.040
amphetamine sulfate	0.148	atropine sulfate	1.047
methamphetamine	0.160	cocaine HCl	1.052
N,N-dimethylamphetamine	0.179	tetracaine HCl	1.063
phenylpropanolamine HCl	0.214	triprolidine	1.097
niacinamide	0.243	tetracosane	1.160
methylephedrine	0.264	phenylbutazone	1.190
MDA HCl	0.309	codeine Phosphate	1.202

MDMA HCl	0.348	morphine sulfate	1.245
benzocaine	0.381	diazepam	1.251
MDEA	0.387	hydrocodone bitartrate	1.259
guaifenesin	0.460	acetylcodeine	1.313
acetaminophen	0.480	monoacetylmorphine	1.327
phenacetin	0.500	oxycodone Base	1.327
methylphenidate	0.548	benzoylecgonine tartrate	1.374
caffeine	0.665	chloroquine phosphate	1.384
carisoprodol	0.699	heroin HCl	1.420
ketamine HCl	0.700	quinine base	1.560
diphenhydramine HCl	0.703	quinine HCl	1.560
antipyrine	0.717	quinidine HCl	1.561
lidocaine HCl	0.721	zolpidem	1.565
doxylamine succinate	0.763	papaverine	1.590
aminopyrine	0.767	clonazepam	1.613
phenobarbital	0.811	hydroxyzine	1.620
xylazine	0.832	alprazolam	1.716
levamisole	0.834	diltiazem	1.727
dipyrone	0.860	noscapine	2.039
procaine HCl	0.891	amoxycillin	not soluble
clenbuterol HCl	0.923	creatine hydrate	not soluble
brompheniramine	0.980	creatinine HCL	not soluble
dextromethorphan	**1.000**	scopolamine HBr	not soluble
methadone HCl	1.007		

3.5. CAPILLARY ELECTROPHORESIS

Method DXM-CE1 (for methorphan)

Injection Solvent:
3.75 mM Sodium Phosphate pH 3.2

Standard Solution Preparation:
Prepare standard solutions of dextromethorphan and levomethorphan at approximately 0.1 mg/ml using the above injection solvent.

Sample Preparation:
Prepare a sample solution so that the concentration approximates the standard concentration using the above injection solvent. If necessary, filter the sample with a 0.45µm filter prior to injection.

Mode: Dynamically coated capillary CE

Column:	CE standard Capillary 50 µm ID, 40 cm LEF
Run Buffer:	Microsolve concentrate for d,l-methorphan: Dilute to 15 parts MeOH-85 parts concentrate
Detector:	UV DAD: 200 nm Reference: 480 nm
Voltage:	20 kV
Cassette Temperature:	15°C
Precondition:	Flush 1.0 min 0.1 NaOH Flush 1.0 min water Flush 1.0 min CElixir A Flush 2.0 min diluted Microsolve concentrate
Injection:	Pressure 35.0 mbar 2.0 sec sample vial Pressure 35.0 mbar 1.0 sec water
Run Time:	5 min
Typical Migration Time:	Dextromethorphan: 3.436 min Levomethorphan: 3.466 min

4. SEPERATION TECHNIQUES

N/A

5. QUANTITATIVE PROCEDURE

5.1. GAS CHROMATOGRAPHY

***Method DXM- GCQ-1* (for methorphan)**

Internal Standard Stock Solution (ISSS):
1 mg/mL of eicosane into $CHCl_3$

Standard Solution Preparation:
Prepare a standard solution of methorphan at 1.0 mg/mL and dilute to volume with the ISSS.

Sample Preparation:
Accurately weigh an amount of sample into an appropriately sized volumetric flask so that the final methorphan concentration is approximately equivalent to that of the standard solution. Dilute to volume with ISSS.

Instrument:	Agilent 6890 Series II (or comparable) gas chromatograph operated in

split mode equipped with a FID detector

Column: 5% Phenyl/95% Methyl silicone gum 12 m x 0.2 mm x 0.33 µm film thickness

Carrier gas: Helium (constant pressure)
Flow: 1.0 mL/min

Temperatures: Injector: 280°C
Detector: 280°C
Oven program:
1) 165°C initial temperature for 2.0 min
2) Ramp to 250°C at 30°C/min
3) Hold final temperature for 1.0 min

Injection Parameters: Split Ratio = 60:1, 1 µL injection

Typical Retention Time: Methorphan: 5.0 min
Eicosane : 4.3 min

Linear Range: 0.215 - 2.15 mg/Ml

Repeatability: RSD less than 3%

Correlation Coefficient: 0.9999

Accuracy: Error less than 5%

COMPOUND	RRT
dimethyl sulfone	0.102
amphetamine	0.142
methamphetamine	0.151
phenylpropanolamine	0.224
ephedrine	0.256
pseudoephedrine	0.258
niacinamide	0.258
MDA	0.354
MDMA	0.423
MDEA	0.480
methorphan	**1.00**
caffeine	0.764
ketamine	0.793

phencyclidine	0.829
eicosane (ISTD)	0.851

6. QUALITATIVE DATA

6.1. HIGH PERFORMANCE LIQUID CHROMATOGRAPHY – MASS SPECTOMETRY

Sample Preparation:
Dissolve a small amount of sample into ammonium formate buffer and methanol. Filter sample with 0.45-micron filter if necessary.

Instrument: High performance liquid chromatograph equipped with diode array and mass spectrometer detector (Agilent 1100 Series SL or equivalent).

Column: Phenomenex Hydro-RP column, 150 mm x 3.0 mm, 80A, 4 µm
Temperature: 40°C

Detector: UV DAD: 210 nm, 10 nm bandwidth
Reference: 450, 100 nm bandwidth
MSD: Scan Mode, single quadrupole with an electrospray ionization source
Polarity: Positive
Fragmentor: 160 V and 260 V

Ionization Mode: API-ES
Drying gas temperature: 350°C
Drying gas flow: 13.0 L/min
Nebulizer Pressure: 30 psi
Capillary Voltage: 4000V
Scan Range: 50-300 m/z

Flow: 0.50 mL/min

Injection Volume: 2.0 µL

Buffer:: 10mM ammonium formate pH 3.7

Mobile Phase: 65% 10mM ammonium formate pH 3.7: 35% acetonitrile

Typical Retention Time: Dextromethorphan in 4.2 min

See spectra on the following pages for LC-MS, FT-IR, FT-Raman, Mass Spectrometry, Nuclear Magnetic Resonance, and Vapor Phase IR.

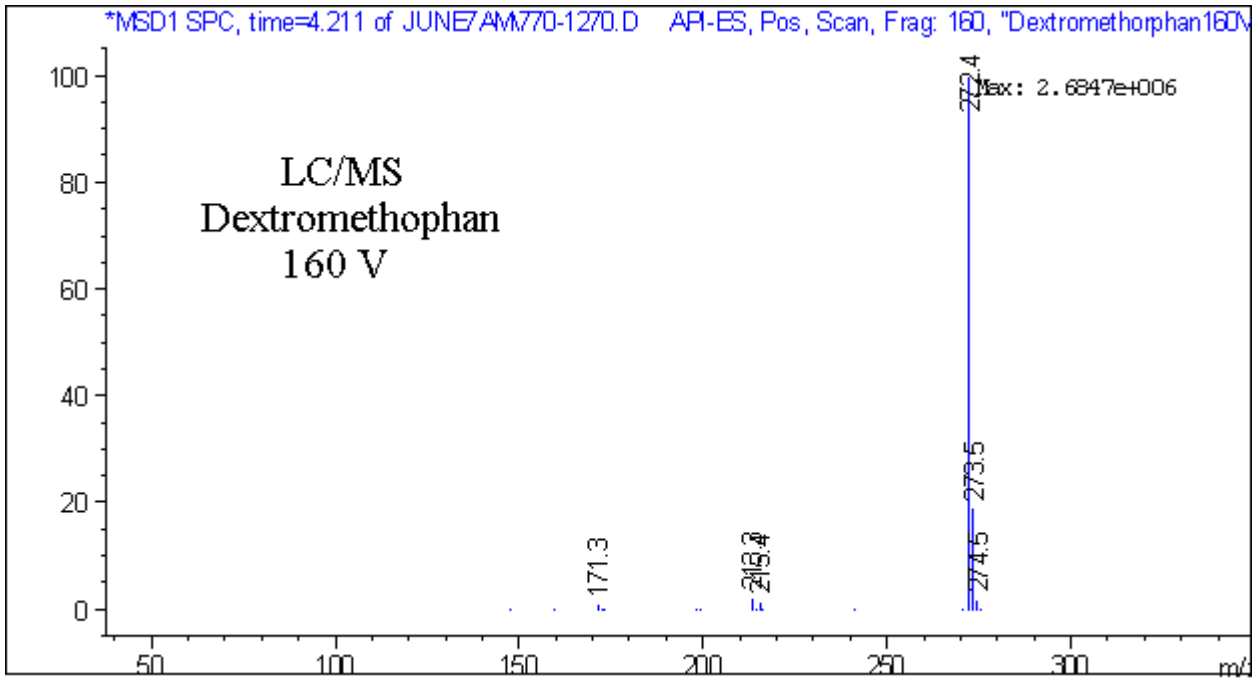
7. REFERENCES

E. G. C. Clarke, “Modern identification of some modern analgesics,” *Bulletin on Narcotics,* 11, No. 1, 27-44 (1959).

Charles C. Fulton, *Modern Microcrystal Tests for Drugs,* Wiley-Interscience, New York, 1969.

8. ADDITIONAL RESOURCES

Wikipedia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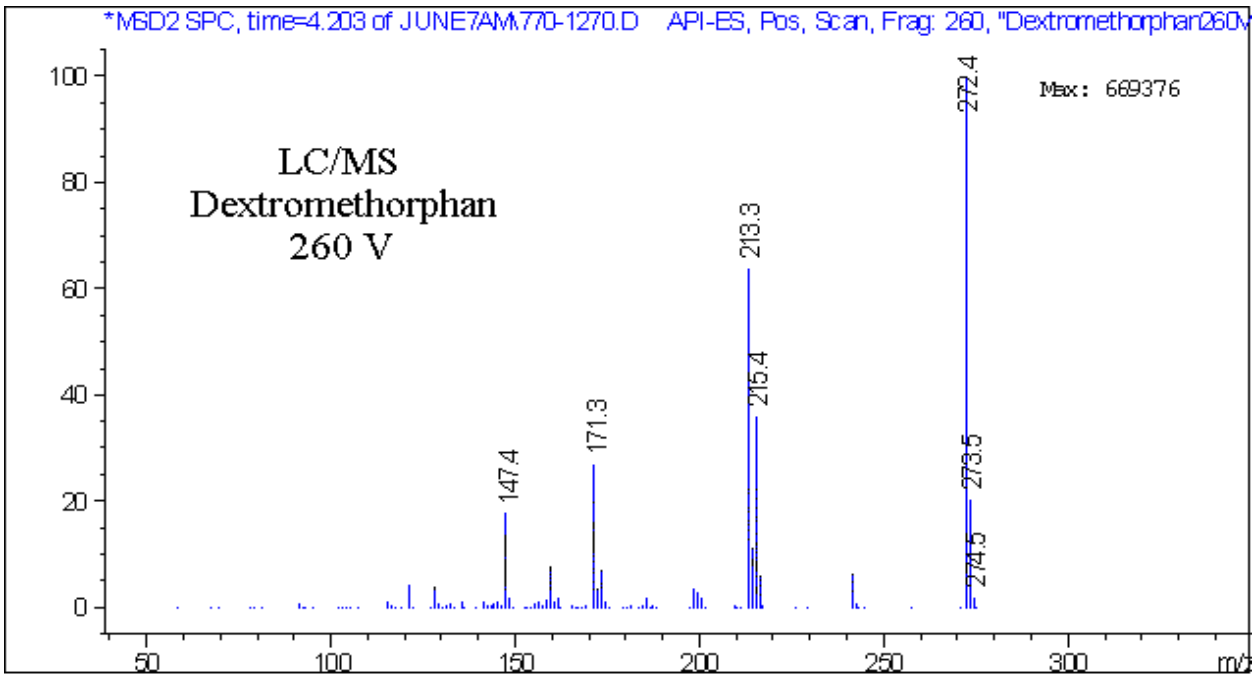
Max: 2.6847e+006
LC/MS
Dextromethophan
160 V
272.4
273.5
274.5
171.3
215.4
100
80
60
40
20
0
50
100
150
200
250
300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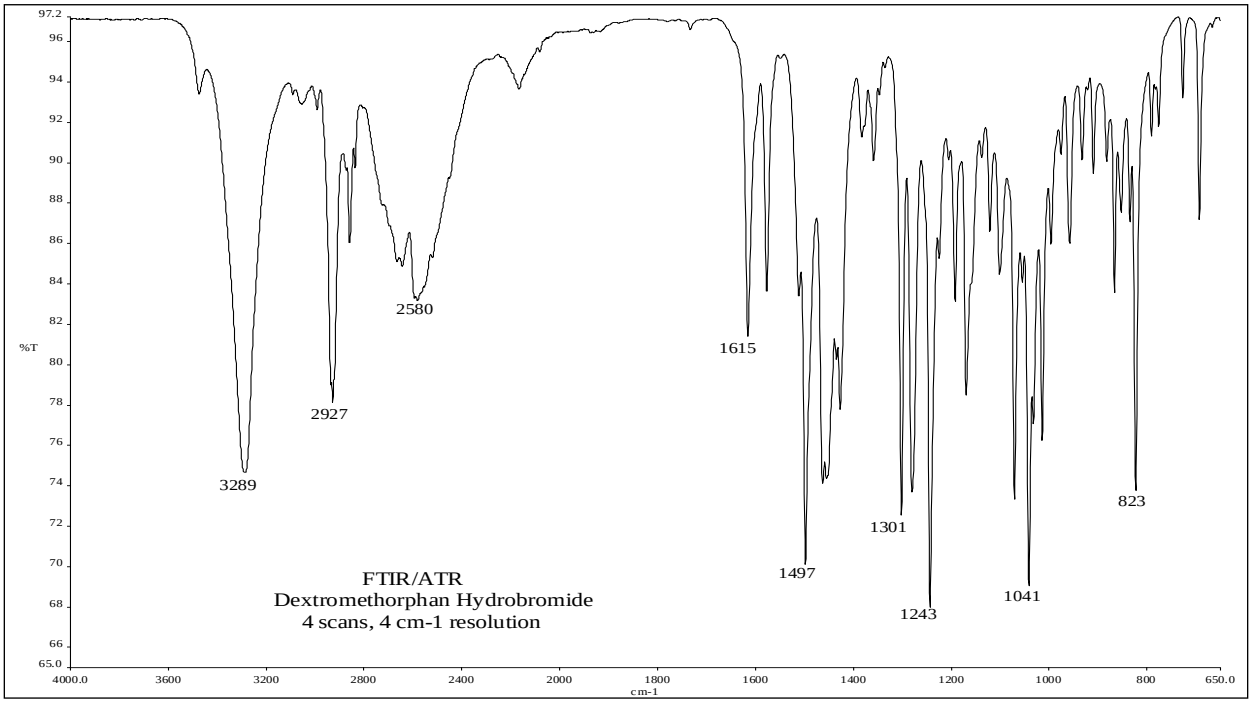
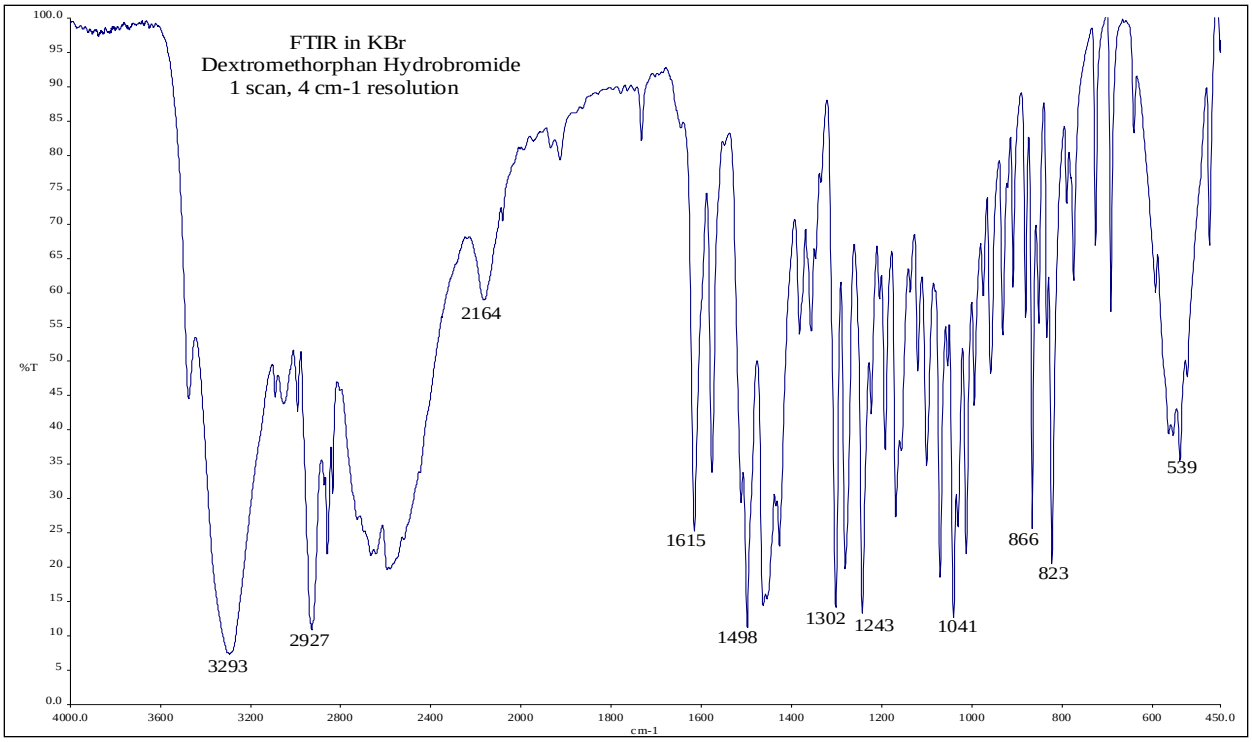
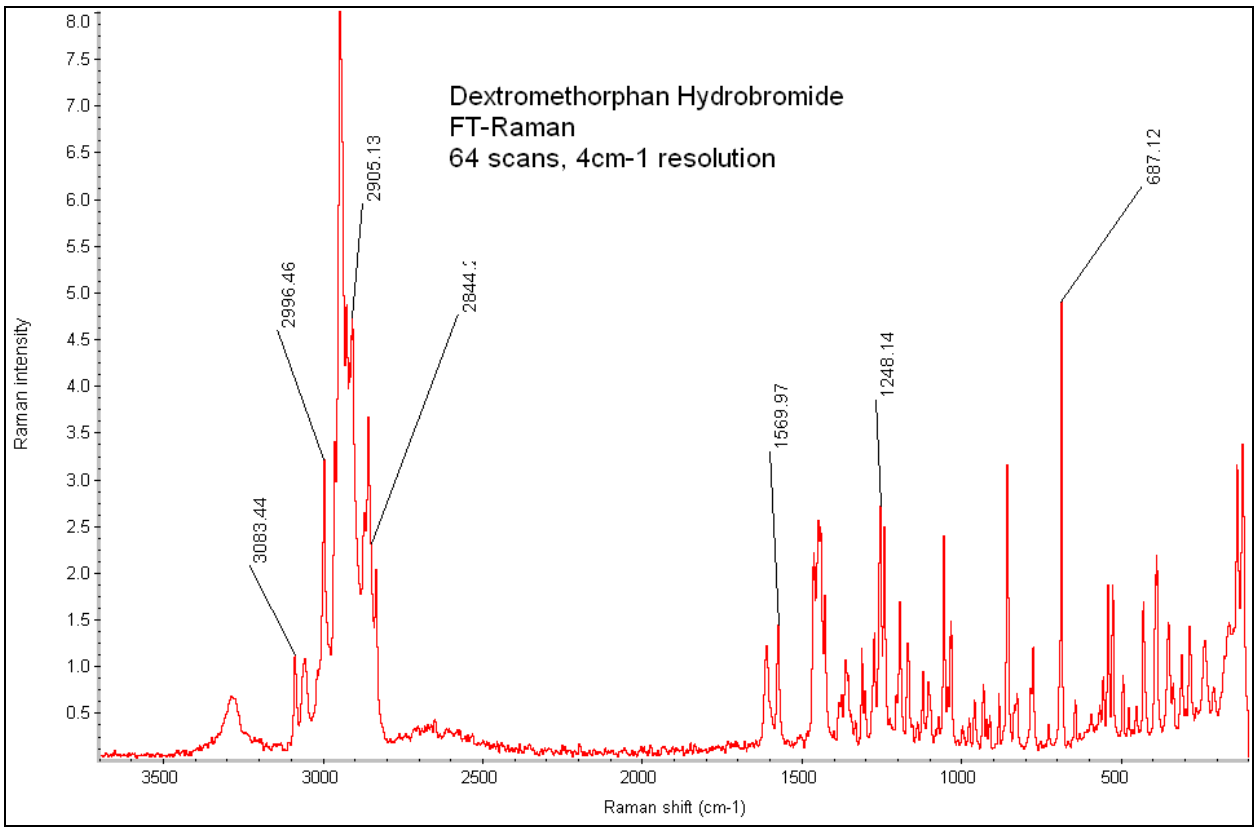
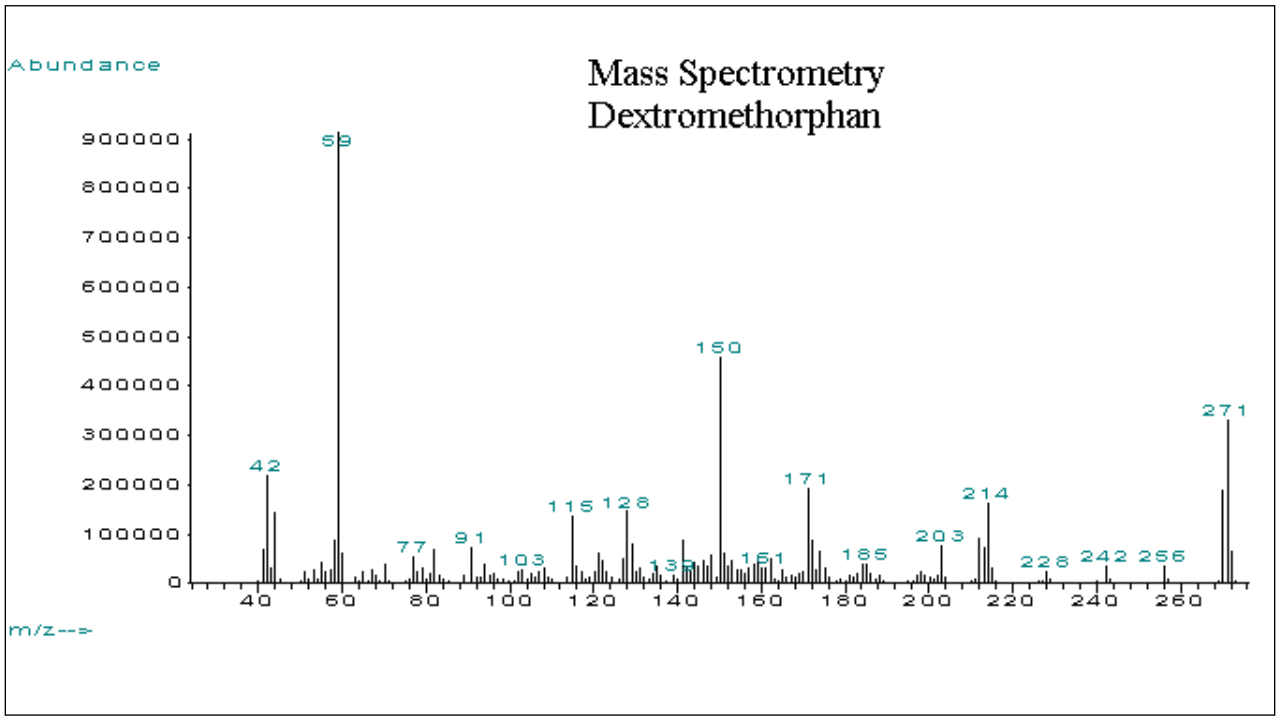
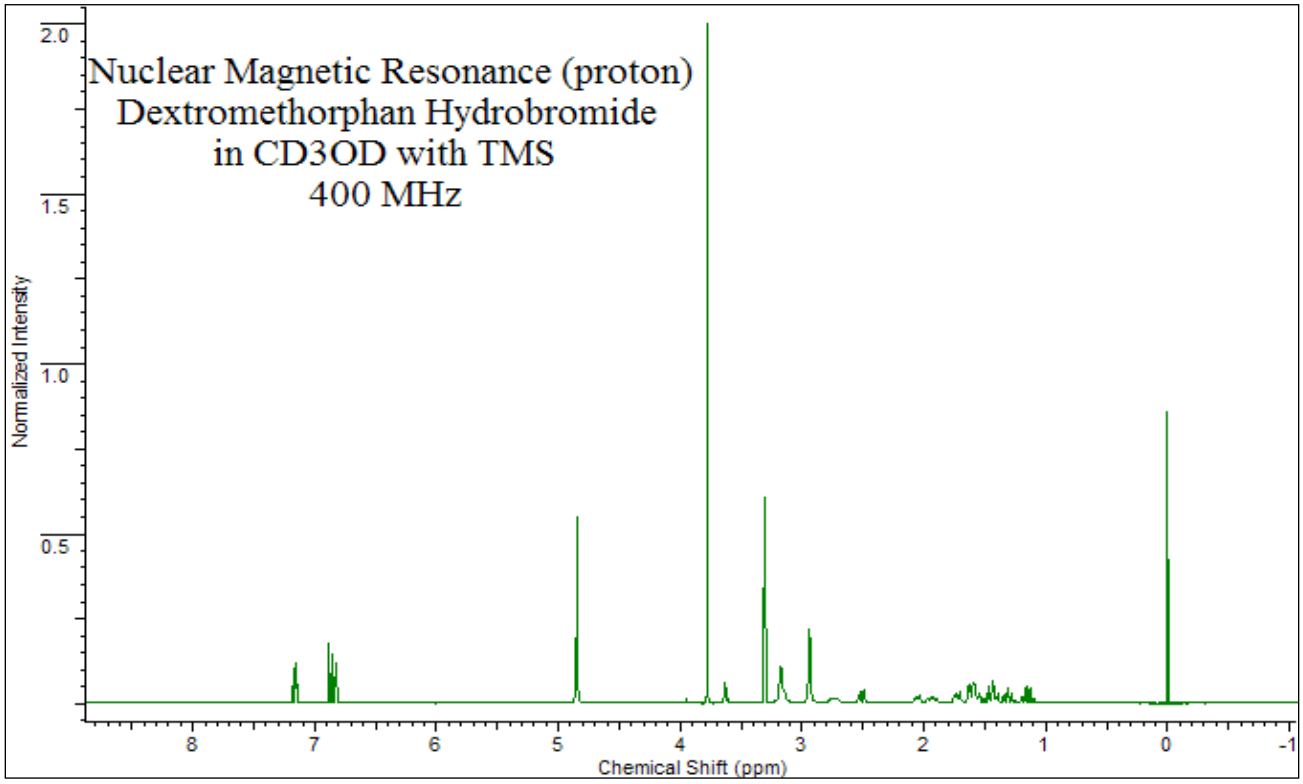
Max: 669376
LC/MS
Dextromethorphan
260 V
272.4
273.5
274.5
213.3
215.4
171.3
147.4
100
80
60
40
20
0
50
100
150
200
250
300

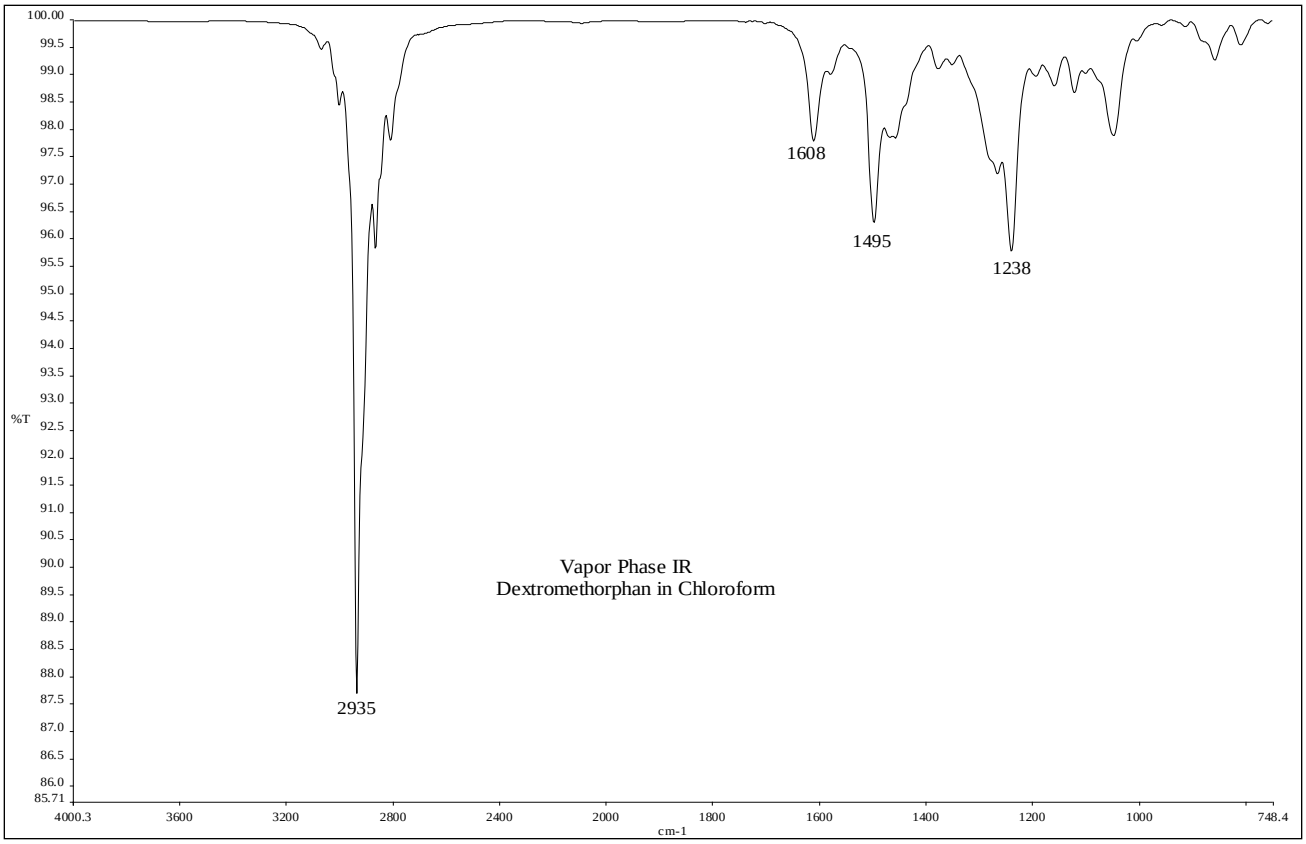

FTIR/ATR
Dextromethorphan Hydrobromide
4 scans, 4 cm-1 resolution
%T
cm-1
3289
2927
2580
1615
1497
1301
1243
1041
823


FTIR in KBr
Dextromethorphan Hydrobromide
1 scan, 4 cm-1 resolution
%T
cm-1
3293
2927
2164
1615
1498
1302
1243
1041
866
823
539


Dextromethorphan Hydrobromide
FT-Raman
64 scans, 4cm-1 resolution
Raman intensity
Raman shift (cm-1)
3083.44
2996.46
2905.13
1569.97
1248.14
687.12


Mass Spectrometry
Dextromethorphan
Abundance
m/z-->


Nuclear Magnetic Resonance (proton)
Dextromethorphan Hydrobromide
in CD3OD with TMS
400 MHz
Normalized Intensity
2.0
1.5
1.0
0.5
8
7
6
5
4
3
2
1
0
-1
Chemical Shift (ppm)


%T
100.00
99.5
99.0
98.5
98.0
97.5
97.0
96.5
96.0
95.5
95.0
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94.0
93.5
93.0
92.5
92.0
91.5
91.0
90.5
90.0
89.5
89.0
88.5
88.0
87.5
87.0
86.5
86.0
85.71
2935
1608
1495
1238
Vapor Phase IR
Dextromethorphan in Chloroform
4000.3
3600
3200
2800
2400
2000
1800
1600
1400
1200
1000
748.4
cm-1