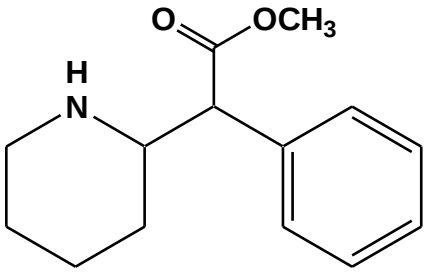
METHYLPHENIDATE

Latest Revision: June 23, 2005



1. SYNONYMS

CFR: Methylphenidate

CAS #: Base: 113-45-1
Hydrochloride: 298-59-9

Other Names: Methyl phenidate
Methyl phenidylacetate
Methyl α-phenyl-α-(2-piperidyl)acetate
Methidate
Ritalin
Ciba 4311b
Centedrin

2. CHEMICAL AND PHYSICAL DAT

2.1. CHEMICAL DATA

Form	Chemical Formula	Molecular Weight	Melting Point (°C)
Base	$C_{14}H_{19}NO_2$	233.3	74-75
Hydrochloride	$C_{14}H_{19}NO_2 \cdot HCl$	269.8	224-226

2.2. SOLUBILITY

Form	A	C	E	M	W
Base	S		S		I
Hydrochloride	S	SS		FS	FS

A = alcohol, C = chloroform, E = ether, M = methanol 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 TECHNIQUE

3.1. COLOR TESTS

REAGENT	COLOR PRODUCED
Liebermann's	Orange

3.2. CRYSTAL TESTS

REAGENT	CRYSTAL PRODUCED
PbI_2-KOAc	Rosettes of long blades and rods, somewhat dendritic, and quite transparent[1] Dense rosettes or rosettes of needles[2]

3.3. THIN LAYER CHROMATOGRAPHY

Visualization

Dragendorff	Yellow to brown
Acidified Iodoplatinate	Violet to brown-violet
Ninhydrin	Violet-pink
Acidified potassium permanganate	Yellow brown

COMPOUND	Relative Rf Values		
	System TLC5	System TLC18	System TLC6
Methylphenidate	1.0	1.0	1.0
MDMA	0.68	0.5	0.3
Ephedrine	0.52	0.14	0.14
Pseudoephedrine	0.57	1.5	0.11
Amphetamine	0.75	0.44	0.26

3.4. GAS CHROMATOGRAPHY

Method MPD-GS1

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 (~2 mL). 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: Methylphenidate: 2.84 min
Tetracosane : 5.97 min

COMPOUND	RRT	COMPOUND	RRT
dimethyl Sulfone	0.208	propoxyphene HCl	1.898
amphetamine Sulfate	0.271	atropine Sulfate	1.910
methamphetamine	0.292	cocaine HCl	1.919
N,N-dimethylamphetamine	0.327	tetracaine HCl	1.940
phenylpropanolamine HCl	0.391	triprolidine	2.001
niacinamide	0.443	tetracosane	2.116
methylephedrine	0.481	phenylbutazone	2.170
MDA HCl	0.563	codeine phosphate	2.194
MDMA HCl	0.635	morphine sulfate	2.271
benzocaine	0.696	diazepam	2.283
MDEA	0.705	hydrocodone bitartrate	2.296
guaifenesin	0.840	acetylcodeine	2.395

acetaminophen	0.876	monoacetylmorphine	2.421
phenacetin	0.913	oxycodone base	2.422
methylphenidate	**1.000**	benzoylecgonine tartrate	2.507
caffeine	1.213	chloroquine phosphate	2.526
carisoprodol	1.275	heroin HCl	2.592
ketamine HCl	1.277	quinine base	2.847
diphenhydramine HCl	1.283	quinine HCl	2.847
antipyrine	1.308	quinidine HCl	2.849
lidocaine HCl	1.315	zolpidem	2.856
doxylamine Succinate	1.392	papaverine	2.900
aminopyrine	1.400	clonazepam	2.943
phenobarbital	1.480	hydroxyzine	2.956
xylazine	1.519	alprazolam	3.131
levamisole	1.521	diltiazem	3.151
dipyrone	1.569	noscapine	3.721
procaine HCl	1.625	amoxycillin	not soluble
clenbuterol HCl	1.685	creatine hydrate	not soluble
brompheniramine	1.788	creatinine HCL	not soluble
dextromethorphan	1.825	scopolamine HBr	not soluble
methadone HCl	1.837		

4. SEPERATION TECHNIQUES

N/A

5. QUANTITATIVE PROCEDURE

***5.1.* GAS CHROMATOGRAPHY**

Method MPD- GCQ-1

Internal Standard Stock Solution (ISSS):
1mg/mL of eicosane into 80:20 $CHCl_3$: MEOH.

Standard Solution Preparation:
Prepare a standard solution of methylphenidate at 1.0mg/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 methylphenidate concentration is approximately equivalent to that of the standard solution. Dilute to volume with ISSS.

Note: Samples and standard must be prepared fresh. Injection port temperatures greater than 200°C result in breakdown of the methylphenidate (observed in ***MPD-GS1***)

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 mL/min

Temperatures: Injector: 200°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 0.5 min

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

Typical Retention Time: Methylphenidate: 3.37 min
Eicosane : 4.42 min

Linear Range: 0.62-2.14 mg/mL

Repeatability: RSD less than 3 %

Correlation Coefficient: 0.9999

Accuracy: Error less than 5%

COMPOUND	RRT
dimethylsulfone	0.155
amphetamine	0.215
methamphetamine	0.237
phenylpropanolamine	0.340
ephedrine	0.388
pseudoephedrine	0.391
niacinamide	0.391
MDA	0.536
MDMA	0.641
MDEA	0.727
methylphenidate	**1.000**
caffeine	1.157
ketamine	1.201

phencyclidine	1.255
eicosane (ISTD)	1.318

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 micron
Temperature: 40°C

Detector: UV DAD: 210nm, 10 nm bandwidth
Reference: 450, 100 nm bandwidth
MSD: Scan Mode, single quadrupole with an electrospray ionization source
Polarity: Positive
Fragmentor: 90 V and 200 V

Ionization Mode: API-ES
Drying gas Temperature 350°C
Drying gas flow 13.0 L/min
Nebulizer Pressure: 30 psi
Capillary Voltage: 4000 V
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: 75% 10mM ammonium formate pH 3.7: 25% acetonitrile

Typical Retention Time: Methylphenidate in 3.8 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

Clarke, E. G. C., “The isolation and Identification of Alkaloids,” in *Methods of Forensic Science*, Vol. I, Frank Lundquist, Ed. Interscience, New York, 1962, p. 127.

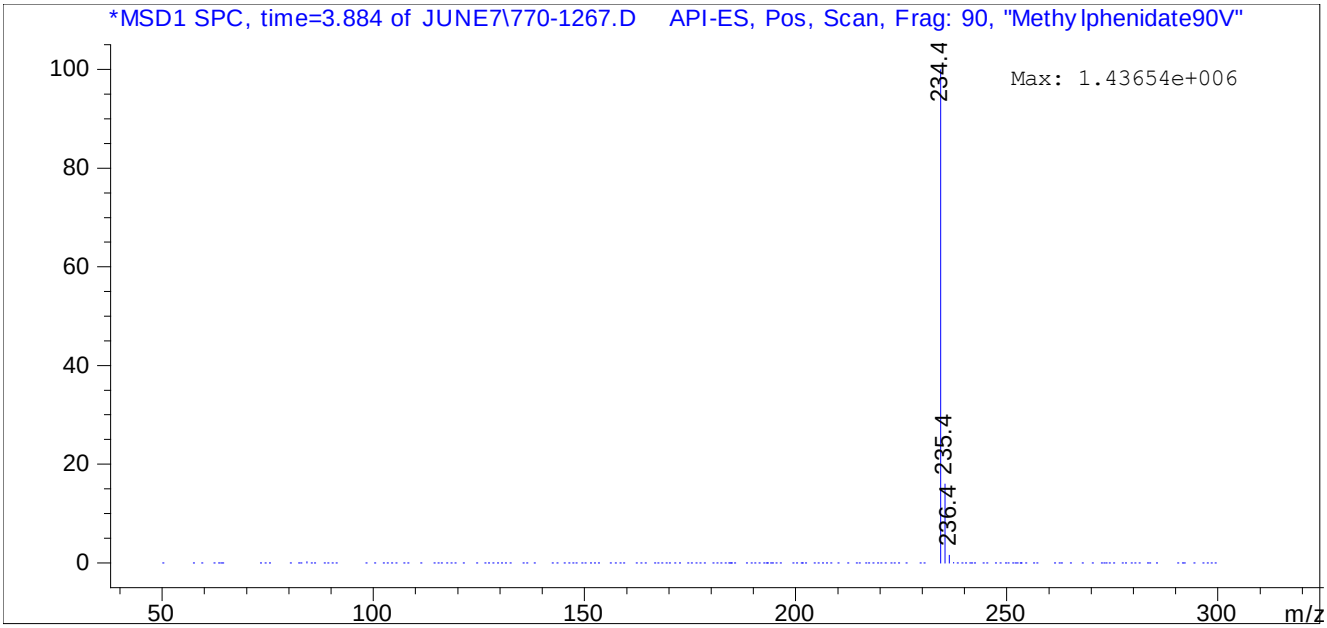
Fulton, Charles C., *Modern Microcrystal Tests for Drugs*, Wiley-Interscience, New York, 1969.

8. ADDITIONAL RESOURCES

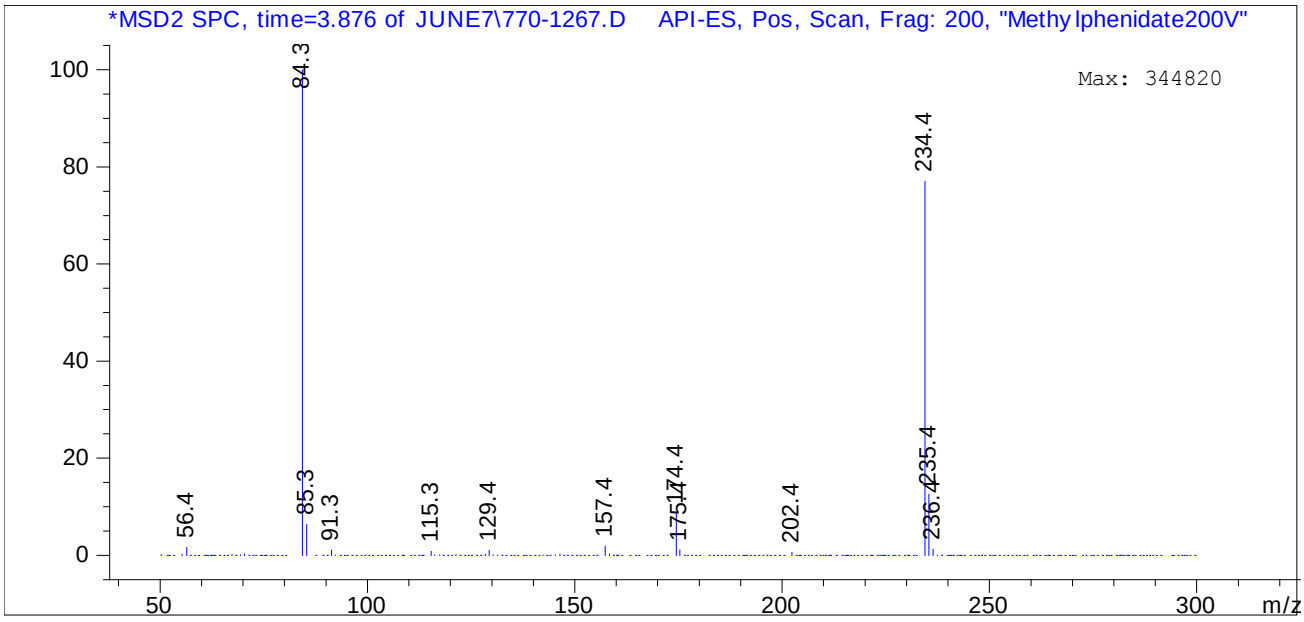
Forendex

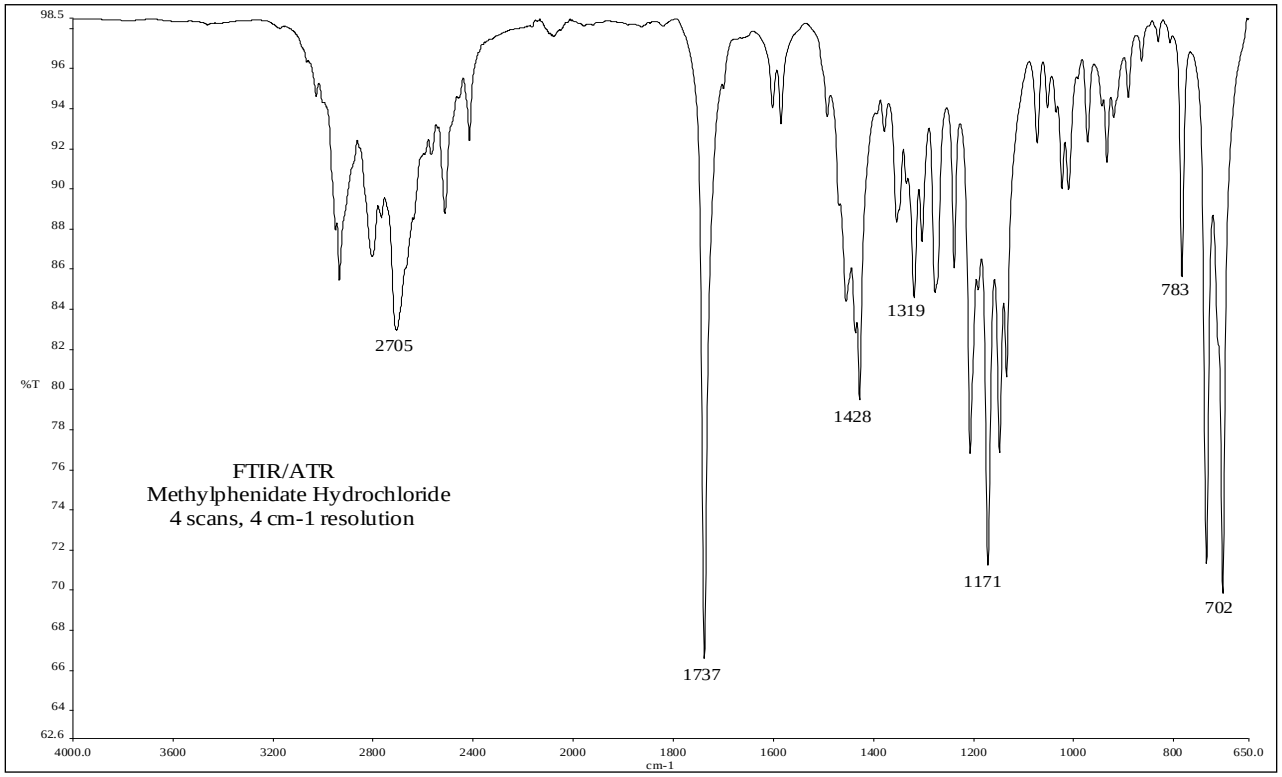
Wikipedia

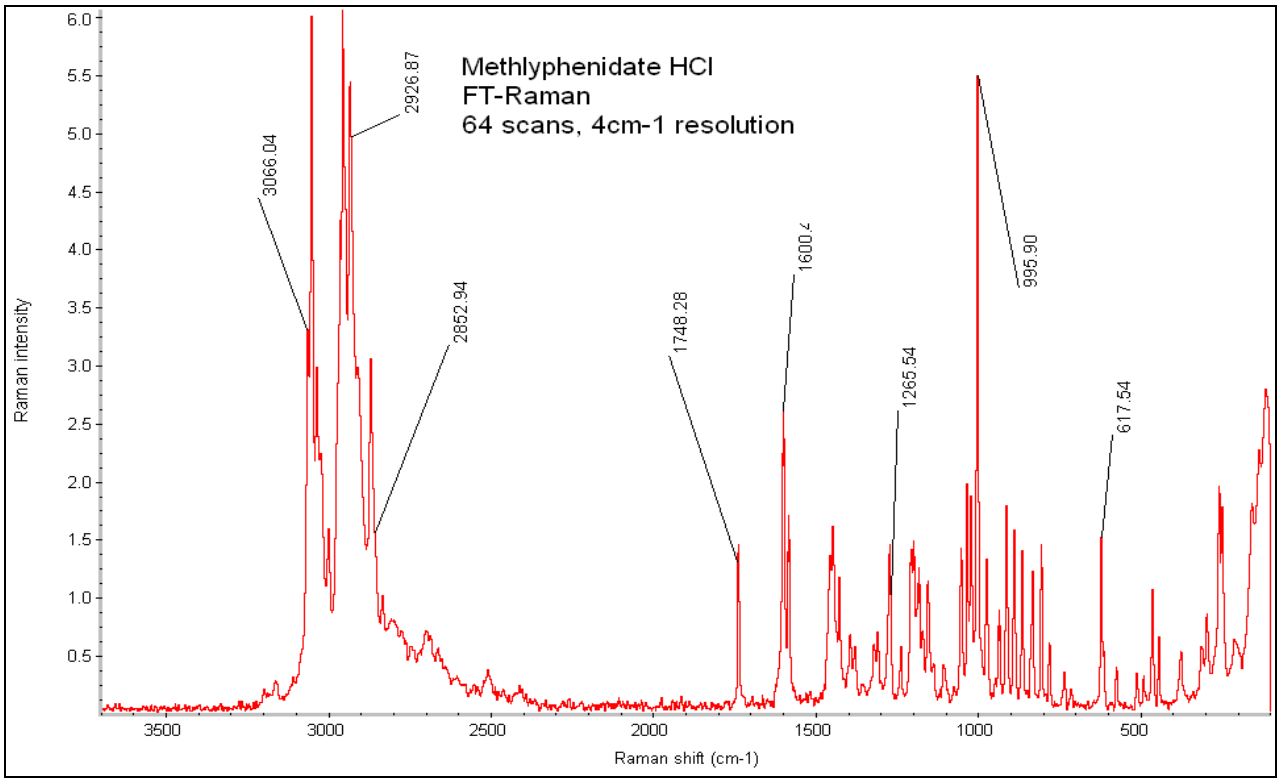
LC/MS: Methylphenidate
90 V

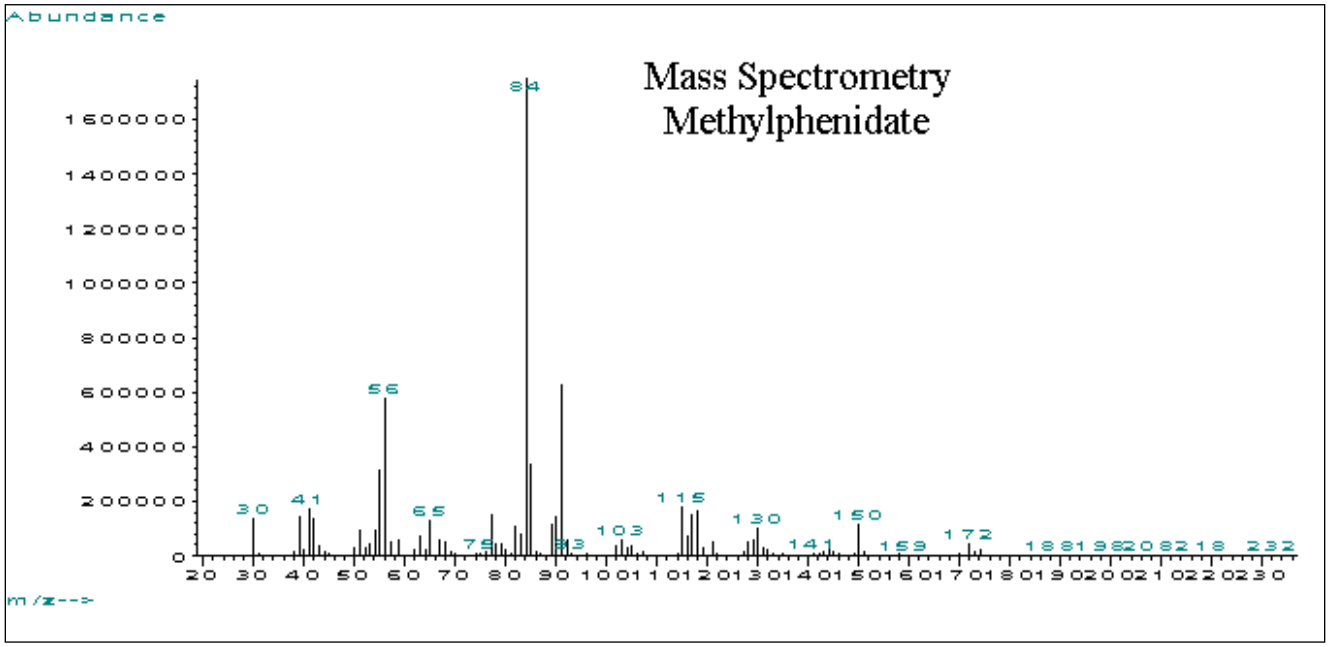


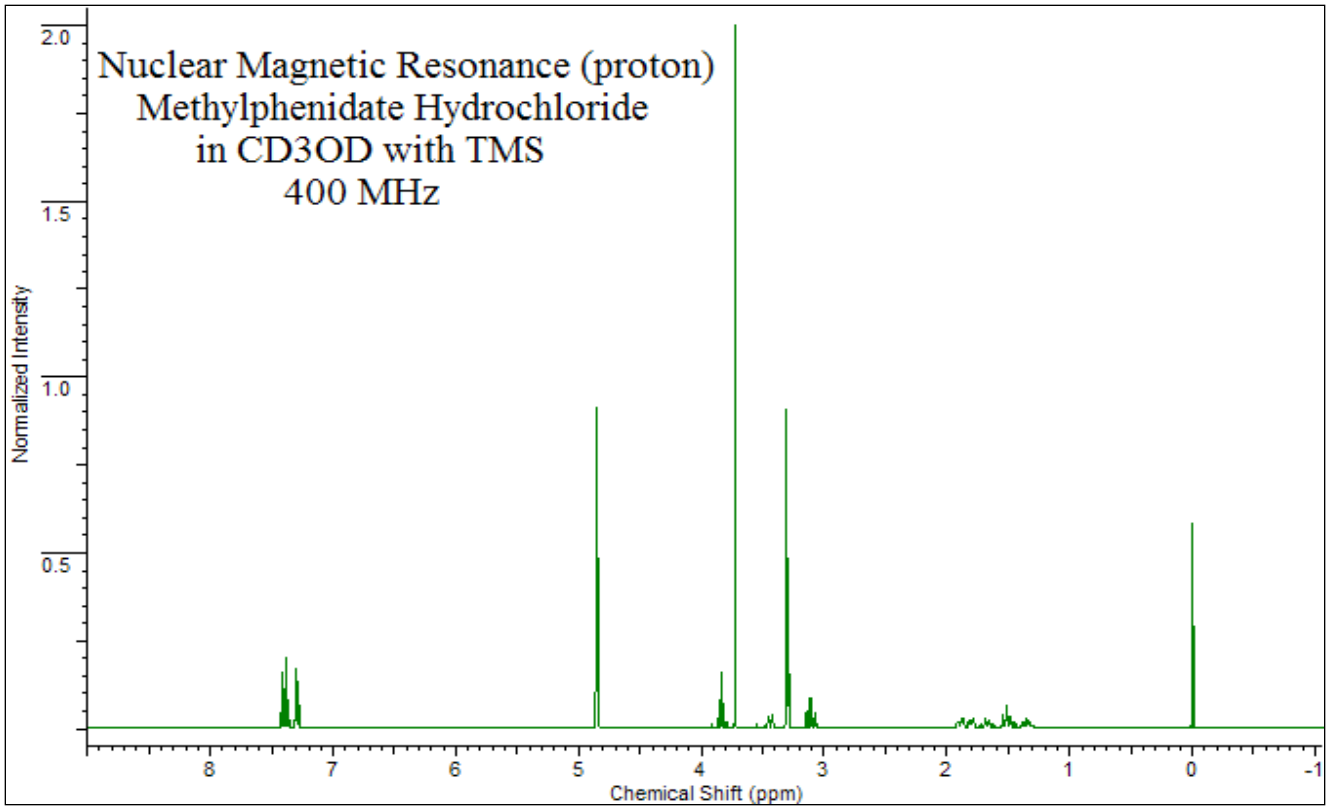
LC/MS: Methylphenidate
200 V

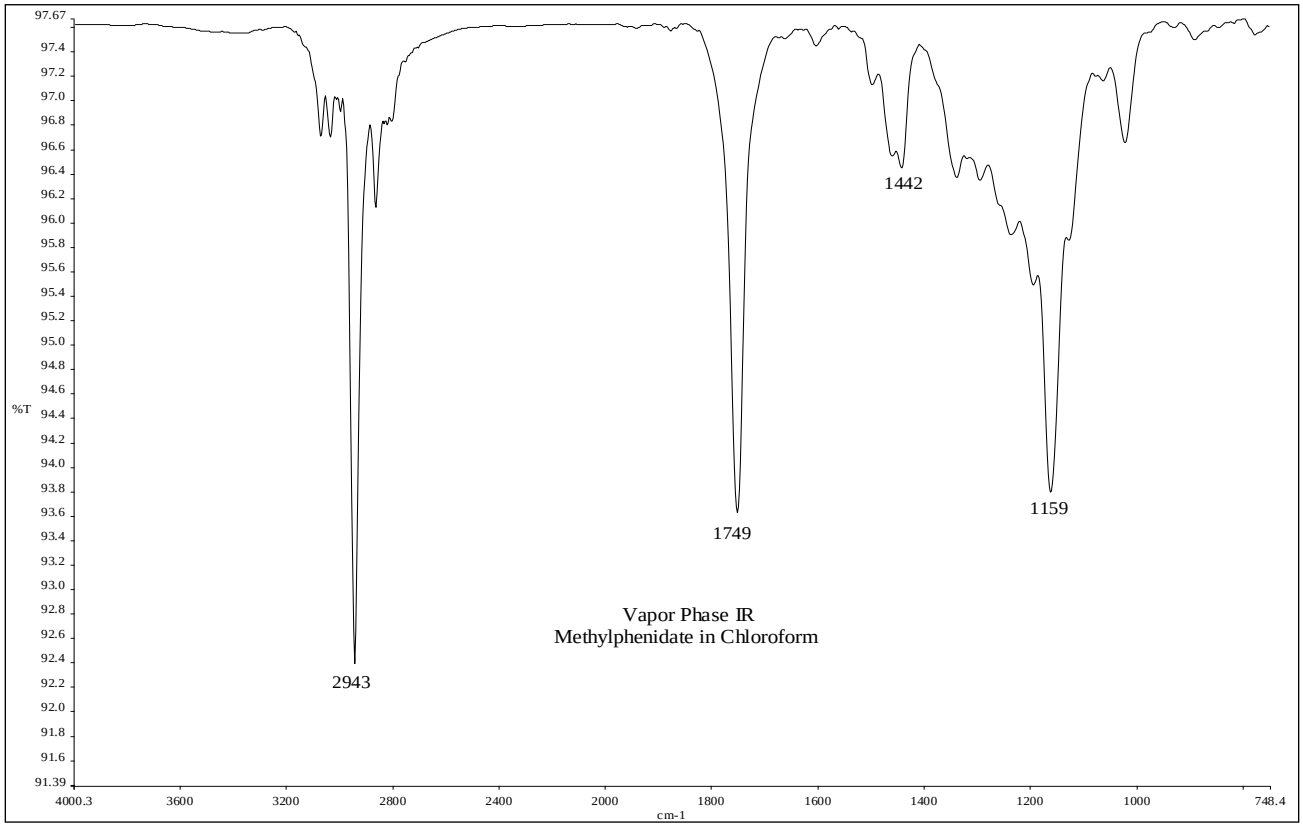



FTIR/ATR
Methylphenidate Hydrochloride
4 scans, 4 cm-1 resolution
%T
cm-1
2705
1737
1428
1319
1171
783
702


Methlyphenidate HCl
FT-Raman
64 scans, 4cm-1 resolution
Raman intensity
Raman shift (cm-1)
3066.04
2926.87
2852.94
1748.28
1600.4
1265.54
995.90
617.54


Abundance
Mass Spectrometry
Methylphenidate
m/z-->


Nuclear Magnetic Resonance (proton)
Methylphenidate Hydrochloride
in CD3OD with TMS
400 MHz
Normalized Intensity
Chemical Shift (ppm)


97.67
97.4
97.2
97.0
96.8
96.6
96.4
96.2
96.0
95.8
95.6
95.4
95.2
95.0
94.8
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%T
94.4
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93.8
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93.4
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93.0
92.8
92.6
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92.0
91.8
91.6
91.39
4000.3
3600
3200
2800
2400
2000
1800
1600
1400
1200
1000
748.4
cm-1
2943
1749
1442
1159
Vapor Phase IR
Methylphenidate in Chloroform