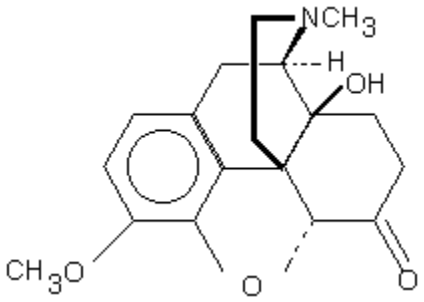
OXYCODONE

Latest Revision: May 16, 2005



1. SYNONYMS

CFR: Oxycodone

CAS #: Base: 76-42-6
Hydrochloride: 124-90-3

Other Names: 7,8-Dihydro-14-hydroxycodeinone
6-Deoxy-7,8-dihydro-14-hydroxy-3-O-methyl-6-oxomorphine
(5α)-4,5-Epoxy-14-hydroxy-3-methoxy-17-methylmorphinan-6-one

Dihydrohydroxycodeinone
14-Hydroxydihydrocodeinone
Dihydrone
Oxycone
Dinarkon
Eubine
Eucodal
Eukodal
Eutagen
Oxikon
Oxycon
Pancodine
Tecodin
Tekodin
Thecodine
Thekodin
Endone
Supeudol
Percocet
Percodan

2. CHEMICAL AND PHYSICAL DATA

2.1. CHEMICAL DATA

Form	Chemical Formula	Molecular Weight	Melting Point (°C)
Base	$C_{18}H_{21}NO_4$	315.4	218-220
Hydrochloride	$C_{18}H_{21}NO_4 \cdot HCl$	351.9	270-272

2.2. SOLUBILITY

Form	A	C	E	H	M	W
Base	***	S	VSS	***	S	VSS
Hydrochloride	***	SS	VSS	***	SS	FS

A = acetone, C = chloroform, E = ether, H = hexane, 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 TECHNIQUES

3.1. COLOR TESTS

REAGENT	COLOR PRODUCED
Marquis	Yellow to brown to violet
Liebermann	Strong bright scarlet
Froehde	Strong brown-yellow
Aldehyde-oxidation H_2SO_4, reagent C-2	Blue

3.2. CRYSTAL TESTS

REAGENT	CRYSTALS FORMED
Platinic bromide in H_2SO_4	Clusters of needles and narrow orange blades
Platinum bromide in HBr-H_2SO_4	Dendritic clusters of narrow orange blades

Platinum bromide in HOAc-H_2SO_4	Blade crystals in clusters from the deposit rim
Iodine-potassium iodide reagent N-1	Brown-red varnish at deposit rim and dark red to black grains, brown birefringent rods
Iodine-potassium iodide reagent M-2	Brown-red varnish at deposit rim, dark red to black grains

3.3. THIN LAYER CHROMATOGRAPHY

Visualization

Dragendorff spray — Acidified iodoplatinate spray
Marquis solution

COMPOUND	Relative R_f		
	System TLC 5	**System TLC 6**	**System TLC 18**
hydromorphone	0.5	0.2	0.1
hydrocodone	0.5	0.4	0.2
codeine	0.7	0.4	0.3
morphine	0.7	0.2	0.0
heroin	0.9	0.7	0.7
oxycodone	1.0	1.0	1.0

3.4. HIGH PERFORMANCE LIQUID CHROMATOGRAPHY

Method OXY-LCS1

Instrument: High performance liquid chromatograph equipped with diode array

Column: 5 µm ODS, 4.6 mm x 150 mm at 50°C

Detector: UV, 280 nm

Flow: 1.0 mL/min

Injection Volume: 10 µL

Buffer: 4000 mL HPLC grade water, 10.0 g sodium hydroxide, 30.0 mL phosphoric acid, 8.0 mL hexylamine, and 0.1 g sodium azide

Mobile Phase: Buffer: acetonitrile 85:15

Samples are to be dissolved in 0.1 N HCl, and then filtered with a 0.45-micron filter.

COMPOUND	RRT
oxycodone	**1.00**
acetaminophen	1.15
caffeine	1.56

4. SEPARATION TECHNIQUES

Dissolve the sample in water and add sodium bicarbonate to make solution moderately basic. Extract the oxycodone base from the aqueous layer with chloroform or other suitable solvent. Filter the chloroform extract through a bed of anhydrous sodium sulfate. Bubble HCl gas through to form the hydrochloride salt.

5. QUANTITATIVE PROCEDURE

***5.1.* HIGH PERFORMANCE LIQUID CHROMATOGRAPHY**

Method OXY-LCQ1

Standard Solution Preparation:
Accurately weigh and prepare a standard solution of oxycodone hydrochloride at approximately 0.5 mg/mL dissolved in 0.1 N HCl. Filter solution through a 0.45-micron syringe filter.

Sample Preparation:
Accurately weigh an amount of sample into a volumetric flask and dilute to volume with 0.1 N HCl. If necessary, dilute the sample so the final concentration approximates the standard concentration or falls within the linear range. Filter solution through a 0.45-micron filter.

Instrument: High performance liquid chromatograph equipped with diode array

Column: 5 µm ODS, 4.6 mm x 150 mm at 50°C

Detector: UV, 280 nm

Flow: 1.0 mL/min

Injection Volume: 10 µL

Buffer: 4000 mL HPLC grade water, 10.0 g sodium hydroxide, 30.0 mL phosphoric acid, 8.0 mL hexylamine, and 0.1 g sodium azide

Mobile Phase: Buffer/acetonitrile 85:15

Typical Retention Time: Oxycodone: 2.40 min

Linear Range: 0.10-2.0 mg/mL

Repeatability: RSD less than 1.0%

Correlation Coefficient: 0.9999

Accuracy: Error less than 5%

COMPOUND	RRT
oxycodone	**1.00 (2.40 min)**
acetaminophen	1.15
caffeine	1.56

5.2. CAPILLARY ELECTROPHORESIS

Method OXY-CEQ

Internal Standard Stock Solution:
1 mg/mL solution containing thiamine hydrochloride in 0.01 N HCl

Standard Solution Preparation:
Accurately weigh standard oxycodone hydrochloride, then add appropriate amount of internal standard stock solution, dilute with 0.01 N HCl so that the oxycodone and thiamine concentrations approximate 0.2 mg/mL.

Sample Preparation:
Accurately weigh sample, add internal standard, then dilute with 0.01 N HCl so that concentrations approximate those of the standard.

Mode: Free Zone

Column: 55 cm x 5 0µm fused silica capillary

Run Buffer: 100 mM lithium phosphate buffer, pH 2.3 (Prepared by titrating 100

	mM phosphoric acid with LiOH to pH 2.3)
Detector:	UV, 207 nm
Voltage:	27 kV
Temperature:	15°C air cooled
Injection:	5 s hydrodynamic at 50 mbar/sec
Run Time:	10 min
Rinse Time:	2.5 min
Linear Range:	0.1-1.9 mg/mL
Repeatability:	RSD of area less than 1.7%
Correlation Coefficient:	0.9999
Accuracy:	Error less than 5%

Note: This method has been validated exclusively for solid dosage units containing oxycodone with acetaminophen.

6. QUALITATIVE DATA

6.1. ULTRAVIOLET SPECTROPHOTOMETER

SOLVENT	MAXIMUM ABSORBANCE (NM)
Hydrochloric acid	280
Sulfuric acid	280

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

7. REFERENCES

Budavari, S., *The Merck Index, 12th Edition*, Merck and Co., Inc., 1996.

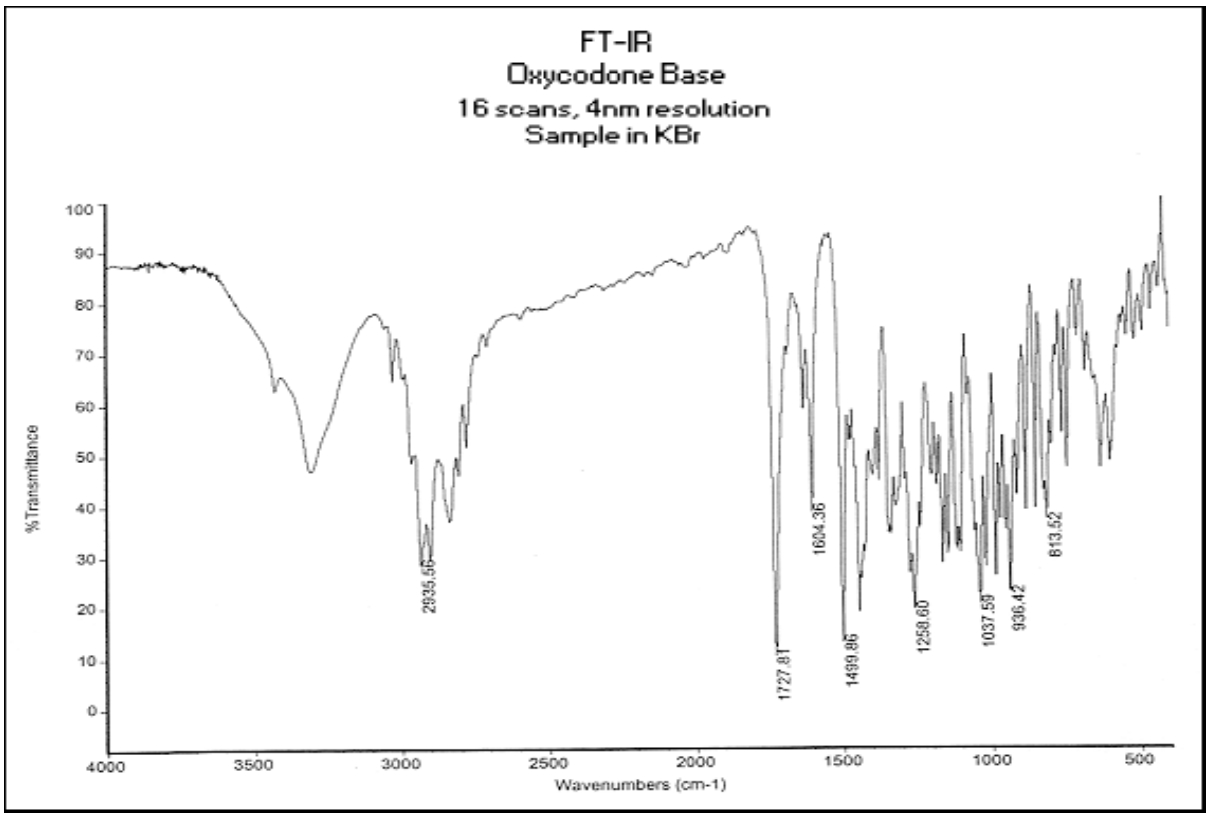
Clarke, E.G.C, *Isolation and Identification of Drugs, 2nd Edition*, The Pharmaceutical Press, 1986.

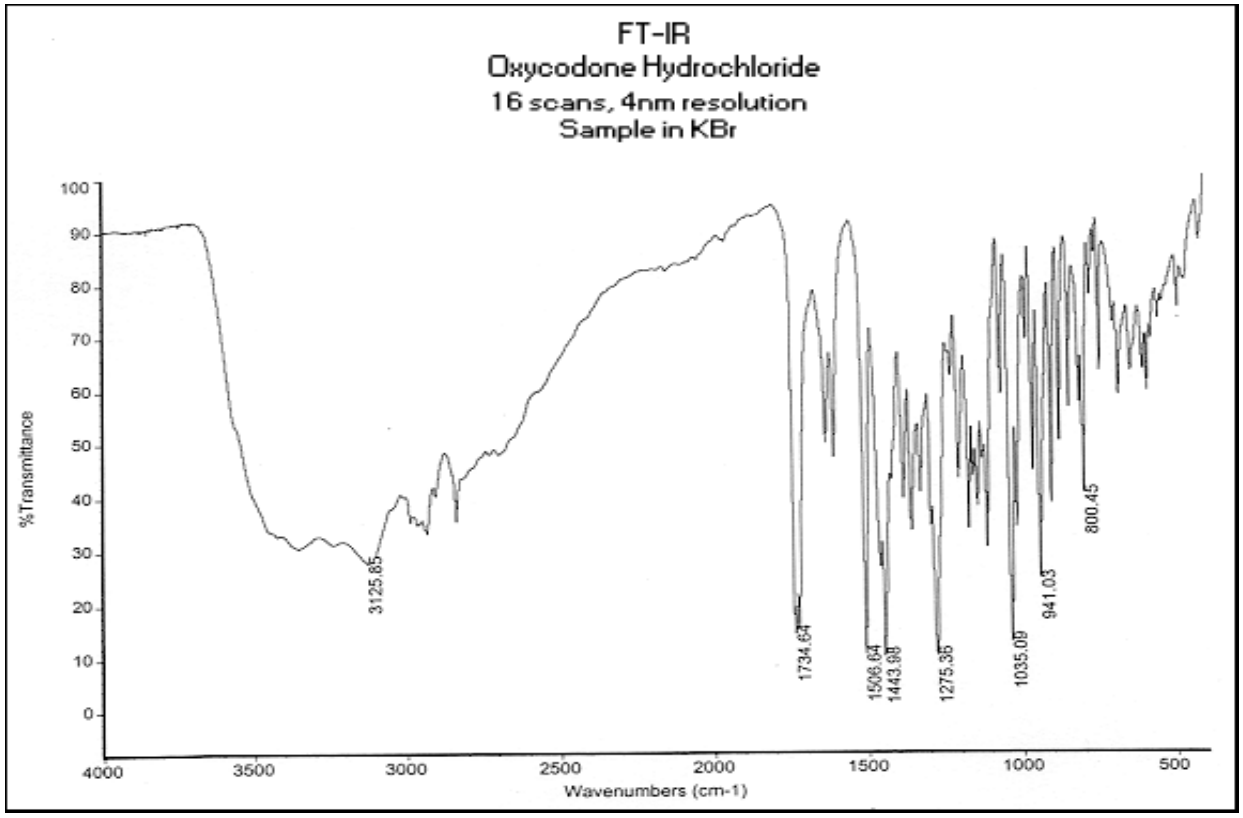
Fulton C.C., *Modern Microcrystal Tests for Drugs*, Wiley-Interscience, 1969.

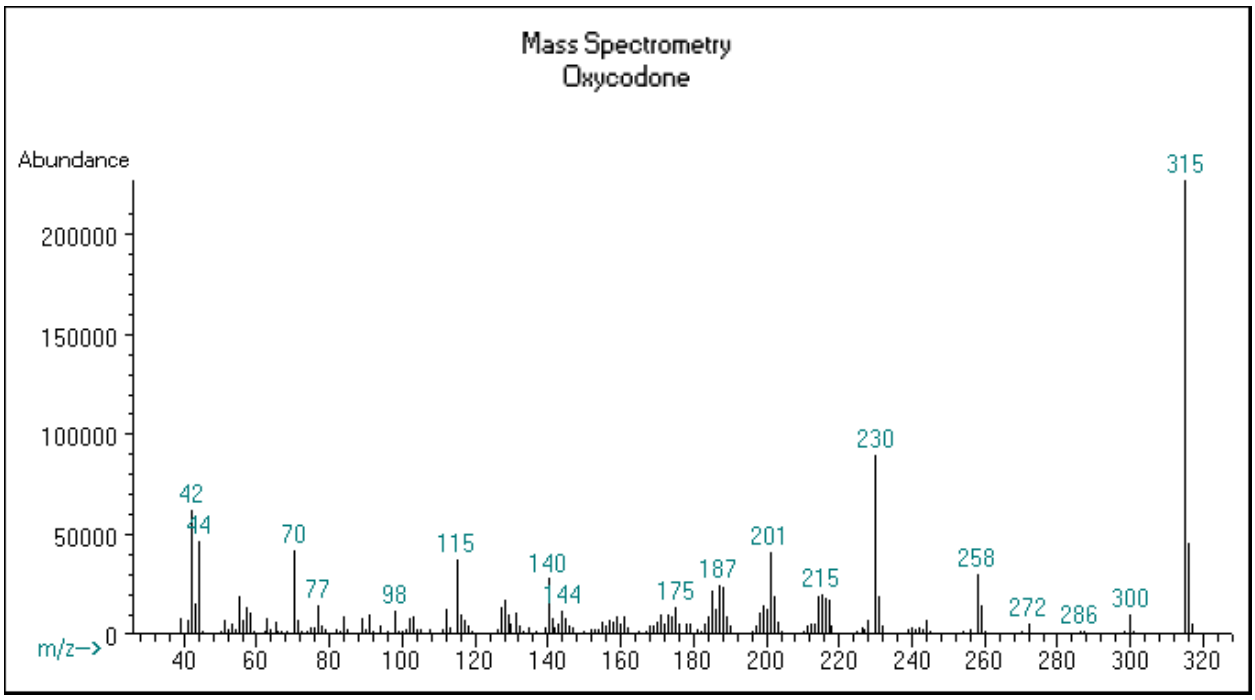
8. ADDITIONAL RESOURCES

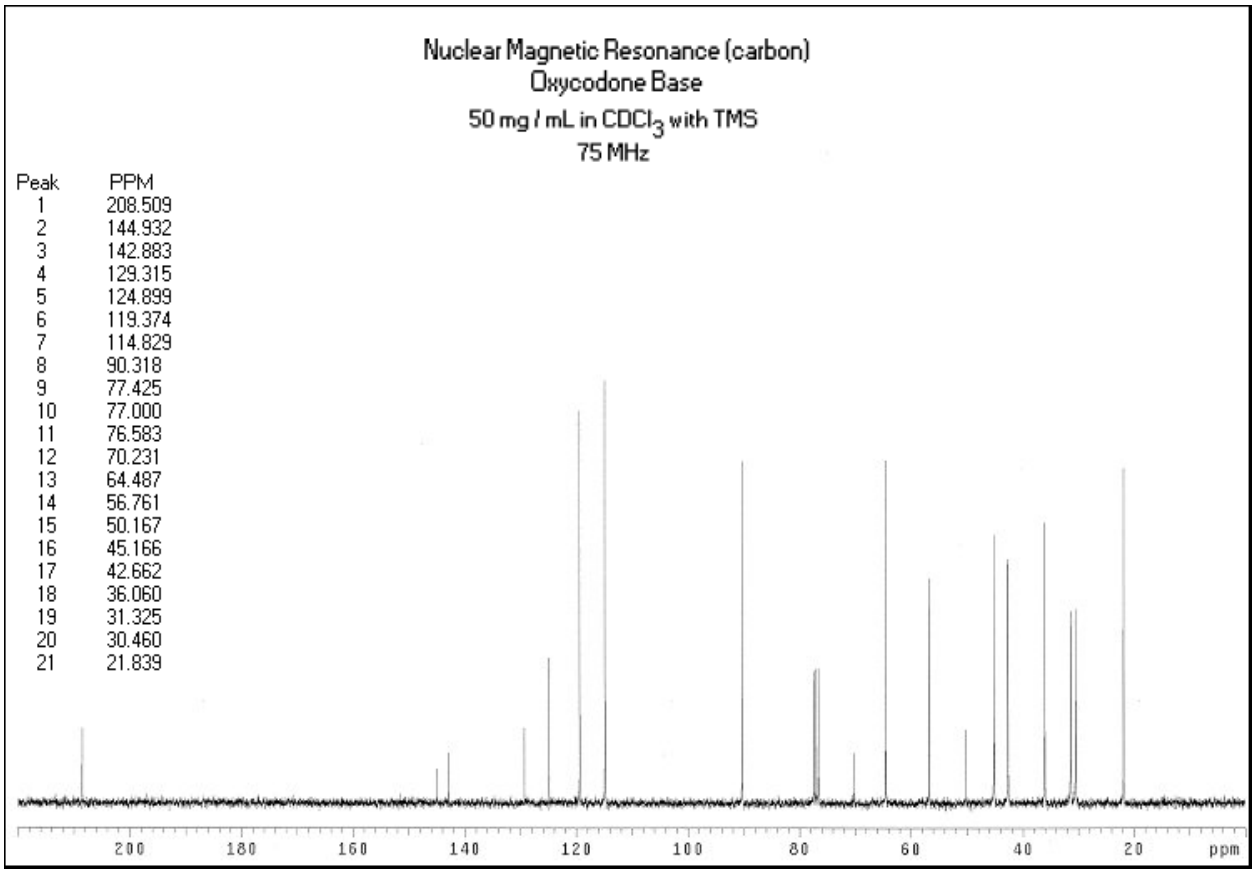
Forendex

Wikipedia


FT-IR
Oxycodone Base
16 scans, 4nm resolution
Sample in KBr
%Transmittance
Wavenumbers (cm-1)
2935.66
1727.81
1604.36
1499.86
1258.60
1037.59
936.42
813.52

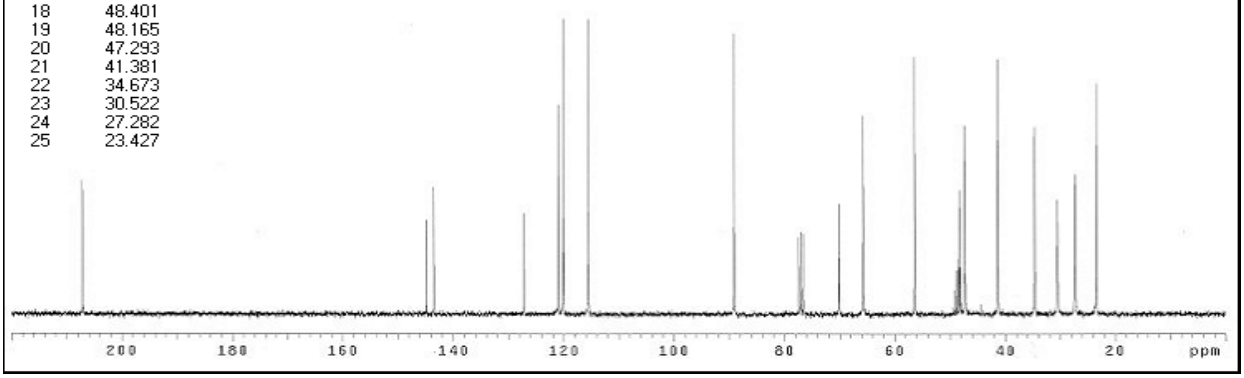

FT-IR
Oxycodone Hydrochloride
16 scans, 4nm resolution
Sample in KBr
%Transmittance
Wavenumbers (cm-1)
3125.85
1734.64
1596.64
1443.98
1275.35
1035.09
941.03
800.45


Mass Spectrometry
Oxycodone
Abundance
200000
150000
100000
50000
0
m/z-->
42
44
70
77
98
115
140
144
175
187
201
215
230
258
272
286
300
315
40
60
80
100
120
140
160
180
200
220
240
260
280
300
320


Nuclear Magnetic Resonance (carbon)
Oxycodone Base
50 mg / mL in CDCl3 with TMS
75 MHz
Peak PPM
1 208.509
2 144.932
3 142.883
4 129.315
5 124.899
6 119.374
7 114.829
8 90.318
9 77.425
10 77.000
11 76.583
12 70.231
13 64.487
14 56.761
15 50.167
16 45.166
17 42.662
18 36.060
19 31.325
20 30.460
21 21.839
200
180
160
140
120
100
80
60
40
20
ppm

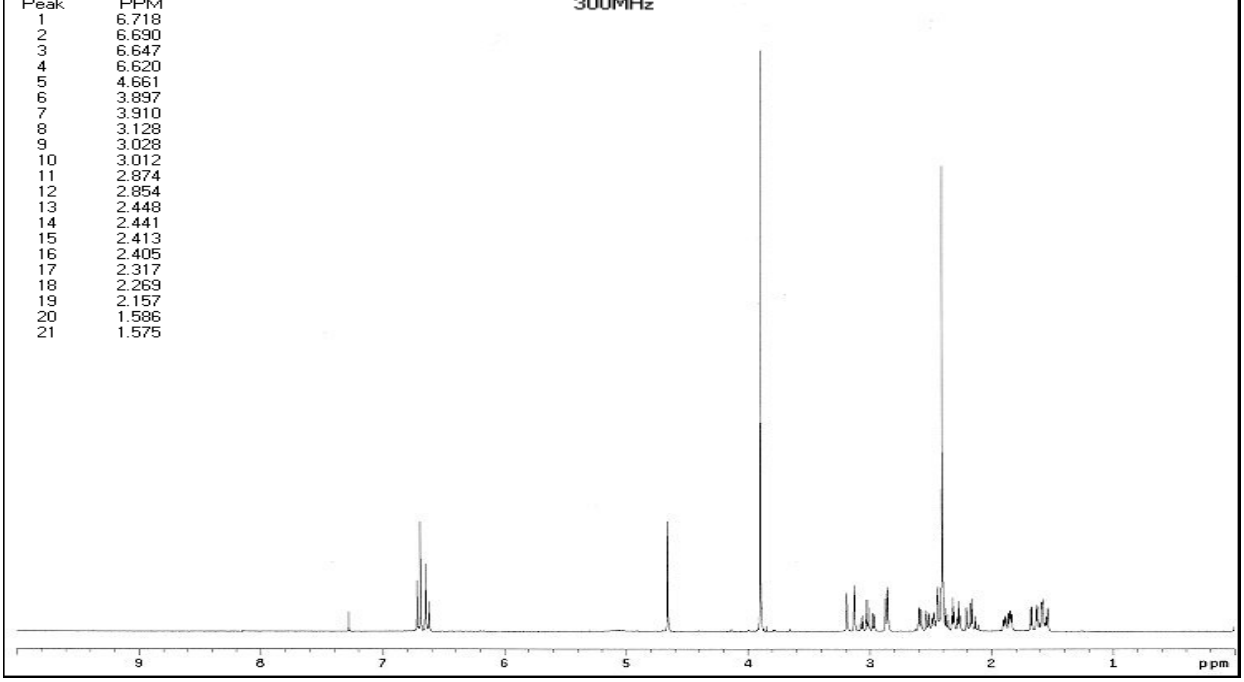
Nuclear Magnetic Resonance (carbon)
Oxycodone Hydrochloride
50 mg / mL in $CDCl_3$ / CD_3OD with TMS
75 MHz

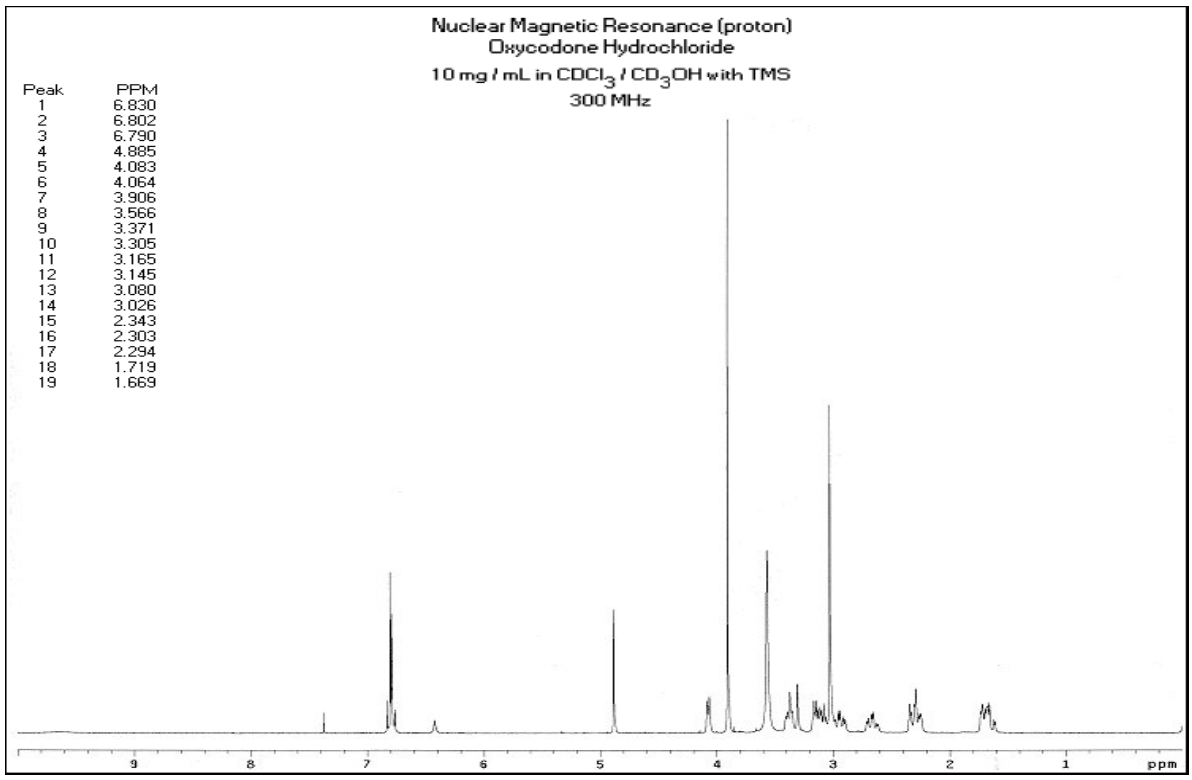
Peak	PPM
1	207.167
2	144.759
3	143.462
4	127.131
5	120.992
6	120.074
7	115.798
8	89.113
9	77.434
10	77.009
11	76.584
12	70.172
13	70.096
14	65.733
15	56.407
16	48.970
17	48.689
18	48.401
19	48.165
20	47.293
21	41.381
22	34.673
23	30.522
24	27.282
25	23.427

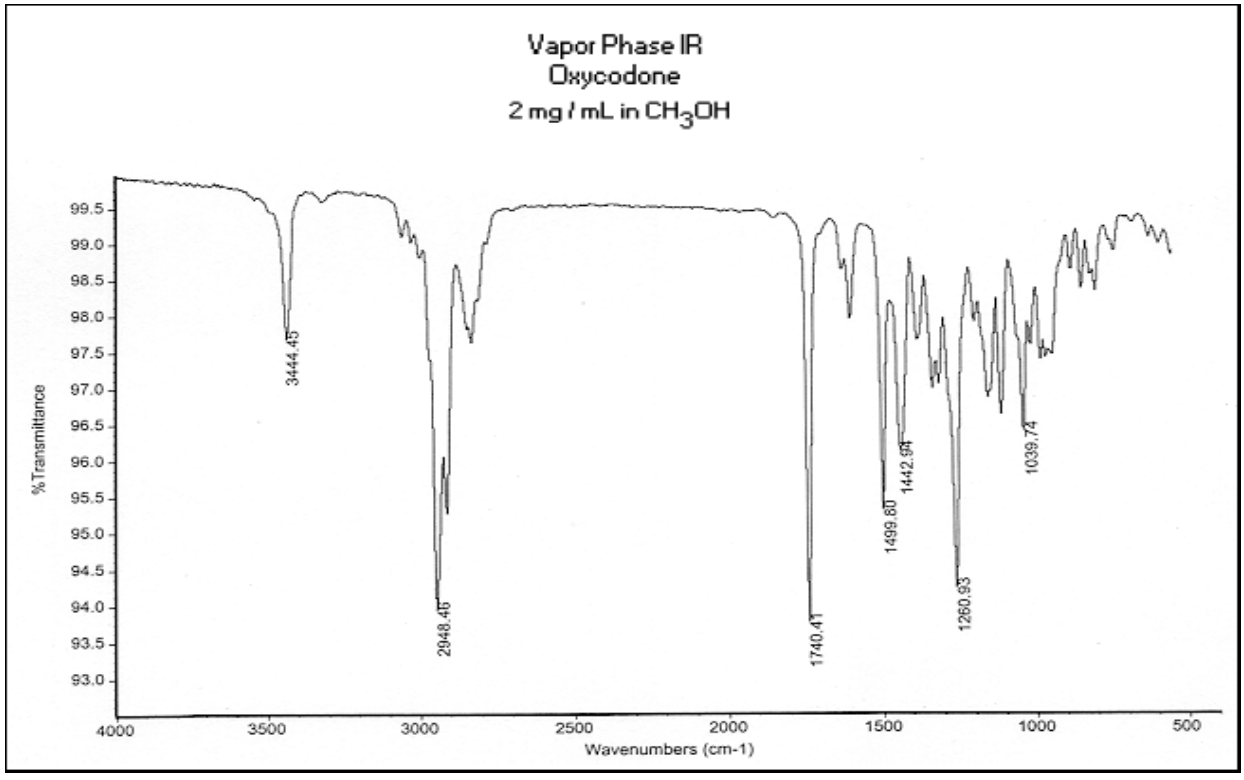


Nuclear Magnetic Resonance (proton)
Oxycodone Base
10 mg / mL in $CDCl_3$ with TMS
300MHz

Peak	PPM
1	6.718
2	6.690
3	6.647
4	6.620
5	4.661
6	3.897
7	3.910
8	3.128
9	3.028
10	3.012
11	2.874
12	2.854
13	2.448
14	2.441
15	2.413
16	2.405
17	2.317
18	2.269
19	2.157
20	1.586
21	1.575




Nuclear Magnetic Resonance (proton)
Oxycodone Hydrochloride
10 mg / mL in $CDCl_3$ / CD_3OH with TMS
300 MHz
Peak PPM
1 6.830
2 6.802
3 6.790
4 4.885
5 4.083
6 4.064
7 3.906
8 3.566
9 3.371
10 3.305
11 3.165
12 3.145
13 3.080
14 3.026
15 2.343
16 2.303
17 2.294
18 1.719
19 1.669
9
8
7
6
5
4
3
2
1
ppm


Vapor Phase IR
Oxycodone
2 mg / mL in CH_3OH
%Transmittance
99.5
99.0
98.5
98.0
97.5
97.0
96.5
96.0
95.5
95.0
94.5
94.0
93.5
93.0
3444.45
2948.40
1740.41
1499.80
1442.94
1260.93
1039.74
4000
3500
3000
2500
2000
1500
1000
500
Wavenumbers (cm-1)