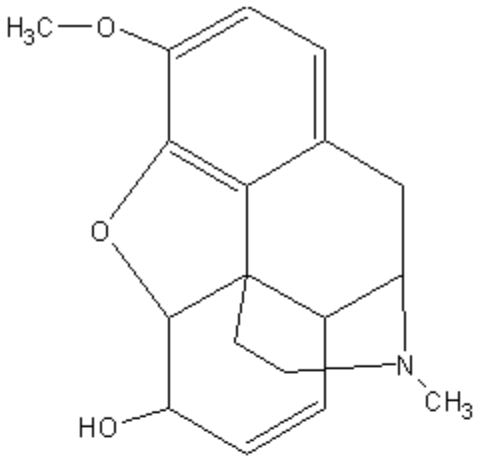
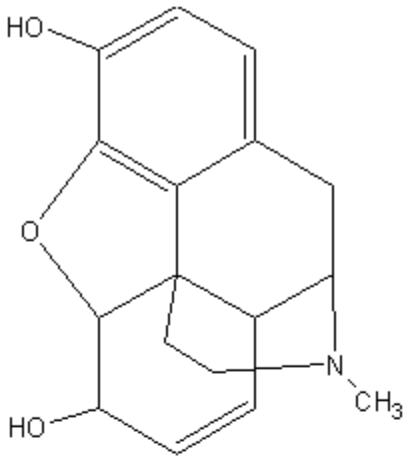
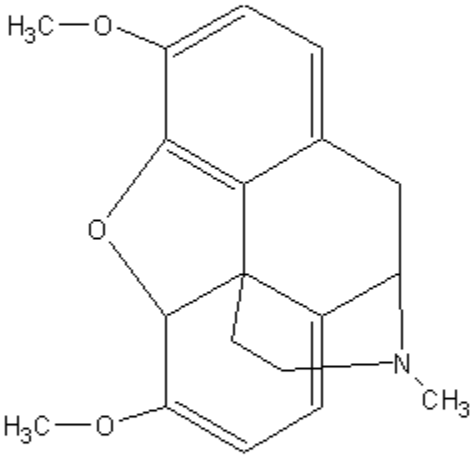


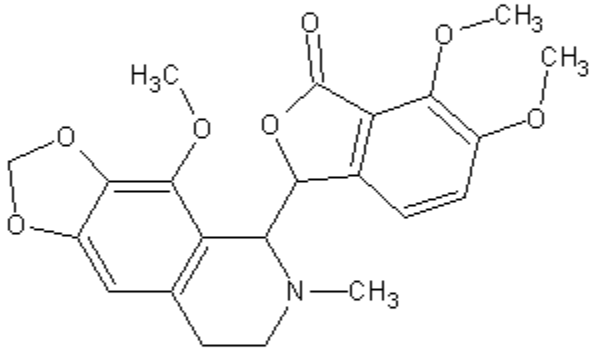
Codeine



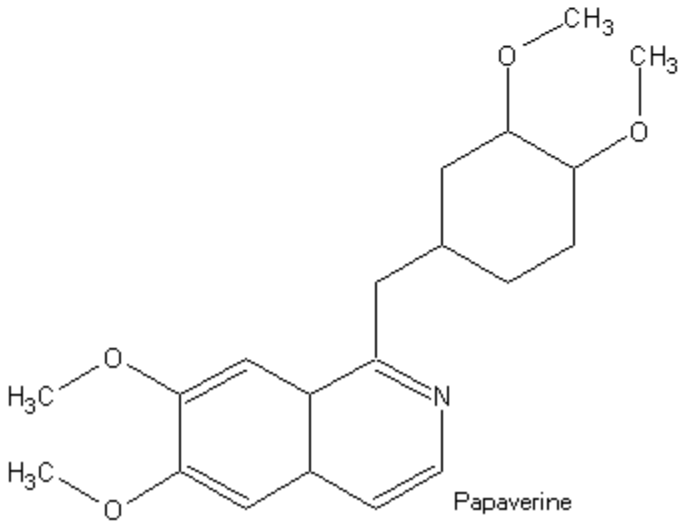
Morphine



Thebaine



Noscapine



Papaverine

1. SYNONYMS

CFR:	Opium
CAS #:	Codeine Base: 76-57-3 Codeine Hydrochloride: 1422-07-7 Morphine Base: 57-27-2 Morphine Hydrochloride: 52-26-6 Thebaine Base: 115-37-7 Noscapine Base: 128-62-1 Noscapine Hydrochloride: 912-60-7 Papaverine Base: 58-74-2 Papaverine Hydrochloride: 61-25-6
Other Names:	Oil poppy Opium poppy

2. CHEMICAL AND PHYSICAL DATA

The immediate precursor of heroin is morphine, and morphine is obtained from opium. Opium is the dried milky juice (latex) obtained from the unripe seed pods of Papaver somniferum L., more commonly referred to as the opium poppy or oil poppy. Morphine has also been reported to be present in *Papaver setigerum*, and as a minor alkaloid in *Papaver decaisnei* and *Papaver rhoeas*. However, there is no known instance of these poppies being used for opium production, and work that is more recent has cast considerable doubt as to the presence of morphine in *Papaver rhoeas*. A major review by Kapoor on the botany and chemistry of the opium poppy is recommended additional reading.

Opium latex is obtained from the seed capsule of the poppy while the capsule is still in the green stage, usually seven or more days after flowering and petal fall. Physically, the opium latex is contained within laticiferous vessels, which lie just beneath the epicarp of the seed capsule. The latex is harvested by making a series of shallow incisions through the epicarp, which allows the latex to "bleed" onto the surface of the seed capsule. Most commonly, the latex is allowed to partially dry on the capsule surface, and is then removed by scraping the capsule with specially designed hand tools. The dried latex is a malleable gum, which is light to dark brown in color, and is known as raw opium. The major constituents of raw opium are plant fragments, resins, sterols, triterpenoid alcohols, fatty acids, alcohols, polysaccharides, and more than thirty alkaloids.

Not all illicitly produced opium is used in the manufacture of heroin, as large quantities of raw opium are used for the production of "prepared opium." The principle use of prepared opium is for smoking. In addition, there are considerable quantities of opium poppy grown for legitimate purposes. These uses include isolation of the opium alkaloids for medicinal purposes, extraction of the oils from the seed, and the use of the seed as food. For instance, a cold pressing of the poppy seed yields a white oil which has been used, in part, as a diluent in olive oil and as a flavoring agent in cooking. A second hot pressing of the seed gives an oil, which has good drying properties and in years past was much used in oil paints and varnishes. Additionally, the use of the poppy seed as a condiment on bakery goods is very widely practiced, and the seed cake, which is left after pressing, is used as an animal food.

Opium is generally encountered in one of four recognized forms: raw opium, prepared opium, opium dross, and medicinal opium.

In its purest form, raw opium is simply dried opium latex; however, it will always contain some quantity of plant fragments as a natural outcome of the harvesting methods employed, and can be cut with, among others things, flour, soil, rosin, or banana pulp. When fresh, it has a tar-like consistency, is very sticky, and is usually a medium brown in color. As raw opium ages, it will gradually become hard and brittle, and the color will become darker, especially at the surface. Distinguishing features of raw opium are its characteristic odor, the presence of plant fragments, and the presence of meconic acid and the porphyroxines.

Prepared opium (also known as cooked opium) is most often produced by dissolving raw opium in hot water, filtering to remove the insoluble materials, and evaporating until the filtrate again becomes a solid paste. This material is prepared almost exclusively for smoking purposes. Prepared opium, like raw opium, will give a positive color test for meconic acid but differs from raw opium in the absence or near absence of plant fragments. Additionally, prepared opium will not give a positive color test for porphyroxine, and the characteristic odor of raw opium is frequently absent.

Opium dross is the residue left after opium has been smoked. There are many local names for dross, for instance, in much of Southeast Asia it is known as "chandu," while in Iran it is known as "sukhteh." Dross is eaten or re-smoked after being added to prepared opium. The presence of dross in prepared opium is generally obvious as a charred material within the prepared opium, and a "burnt" odor is frequently present. Dross does not give a positive color test for either meconic acid or porphyroxine.

Medicinal opium is generally one of three preparations. The first is "granulated" or "powdered" opium (depending upon the final mesh size of the product), and is an opium which has been thoroughly dried at 70° C and diluted with lactose to give a morphine content between 10 and 10.5% (in Germany 9.8 to 10.2%) by weight. A second medicinal opium is known as either “deodorized opium” or “denarcotized opium.” This material is prepared by treating opium with petroleum ether, which removes both narcotine (noscapine) and the characteristic odor of opium. The concentration of morphine in denarcotized opium is also 10 to 10.5% by weight. The third medicinal opium has been modified rather extensively, and is commonly known within the U.S. under the trade name of Pantopon. This preparation is also known as "concentrated opium," Omnopon, or perhaps most commonly, Papaveretum. It is a mixture of morphine, codeine, papaverine, and noscapine as hydrochloride salts, with the morphine content adjusted to approximately 50% by weight.

2.1. CHEMICAL DATA

Form	Chemical Formula	Molecular Weight	Melting Point (°C)
Morphine Base	$C_{17}H_{19}NO_3$	285.3	247-248 (decomposes)
Morphine Base	$C_{17}H_{19}NO_3 \cdot H_2O$	303.4	255-257
Morphine Hydrochloride	$C_{17}H_{19}NO_3 \cdot HCl \cdot H_2O$	375.8	200 (decomposes)
Codeine Base	$C_{18}H_{21}NO_3$	299.3	***
Codeine Base	$C_{18}H_{21}NO_3 \cdot H_2O$	317.4	154-156
Codeine Hydrochloride	$C_{18}H_{21}NO_3 \cdot HCl \cdot 2H_2O$	371.9	280 (decomposes)
Thebaine Base	$C_{19}H_{21}NO_3$	311.4	193

2.2. SOLUBILITY

Form	A	C	E	H	M	W
Morphine Base	SS	VSS	VSS	PS	S	VVS
Morphine Hydrochloride	***	I	I	PS	***	S
Morphine Sulfate	***	I	I	SS	***	S
Codeine Base	FS	VS	FS	FS	FS	SS
Codeine Hydrochloride	***	SS	***	PS	***	S
Codeine Sulfate	***	I	I	VSS	***	S
Thebaine Base	***	VS	SS	VS	***	VSS
Thebaine Hydrochloride	***	S	***	S	***	S

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

Note: Because of the numerous forms of opium and problems associated with matrix effects, the opium alkaloid solubilities may vary dramatically.

3. SCREENING TECHNIQUES

3.1 MICROSCOPIC EXAMINATION

Plant debris can be isolated for microscopic examination by exhaustively washing the opium with water. The residue will contain poppy capsule fragments and occasionally spherical pollen grains with three pores. The poppy capsule fragments are epidermis composed of small 5 to 6 sided cells with strongly thickened walls. Sometimes stellate lumina, anomcytic stomata approximately 17 mm wide by 25 mm long or circular, are also infrequently noted.

3.2. COLOR TESTS

Reagent	Color Produced
Morphine:	
Marquis	Purple violet
Mecke's reagent	Dark green
Froehde's reagent	Purple becoming grey-purple
Codeine:	
Marquis	Purple violet
Mecke's reagent	Green blue
Froehde's reagent	Blue green
Papaverine:	
Marquis	No color
Mecke's reagent	Dark blue
Froehde's reagent	Light green
Noscapine:	
Marquis	Bright yellow
Mecke's reagent	Green blue
Froehde's reagent	Cherry red
Meconic acid:	
10% Ferric chloride	Dirty blood red
Porphyroxine:	
Mineral acids	Intense red color

3.3. CRYSTAL TESTS

Reagent	Crystals Formed
Morphine:	
Potassium cadmium iodide	Sheaves of fine needles
Potassium tri-iodide	Plates
Codeine:	
Potassium cadmium iodide	Gelatinous rosettes changing to aggregates of small tablets
Potassium tri-iodide	Feathery rosettes forming overnight
Thebaine:	
Platinic chloride	Dense rosettes
Sodium carbonate	Rosettes of small plates

3.4. THIN LAYER CHROMATOGRAPHY

Visualization

Dragendorff reagent spray: orange spots on yellow background
Acidified potassium iodoplatinate: blue to purple spots

COMPOUND	Relative R_f		
	System TLC 3	System TLC 4	System TLC 5
morphine	0.2	0.2	0.4
codeine	0.4	0.4	0.3
papaverine	0.7	0.7	0.6
noscapine	0.9	0.8	0.7

3.5. GAS CHROMATOGRAPHY

Analysis of opium by gas chromatography may be problematic. Thebaine undergoes extensive rearrangement and decomposition in the injection port and morphine requires derivatization prior to analysis.

Method OPI-GCS1

Instrument: Gas Chromatograph operated in split mode with FID

Column: DB-1 30 m x 0.2 mm x 0.25 µm film thickness

Carrier gas: Hydrogen at 1.1 mL/min

Temperatures: Injector: 280°C
Detector: 280°C
Oven program:
1) 205°C initial temperature for 1.0 min
2) Ramp to 275°C at 11.5°C/min
3) Hold final temperature for 8.91 min

Injection Parameters: Split Ratio = 25:1, 1 µL injected

Samples are to be dissolved in 4:1 chloroform: methanol and filtered.

COMPOUND	RRT	COMPOUND	RRT
nicotinic acid	0.24	methapyrilene	0.63
nicotinamide	0.28	procaine	0.65
dimethylphthalate	0.30	stearic acid	0.75
salicylamide	0.30	dextromethorphan	0.78
barbital	0.31	methadone	0.78
aminorex	0.34	amitryptyline	0.83
methylaminorex	0.34	promethazine	0.90
allobarbital	0.35	acetylated dipyrone	0.92
ibuprofen	0.36	scopolamine	0.93
acetaminophen	0.38	acetylprocaine	0.95
butalbital	0.38	phenylbutazone	0.98
guaifenesin	0.38	**codeine**	**1.00 (6.61 min)**
phenacetin	0.39	tetracosane	1.00
amobarbital	0.41	ethylmorphine	1.03
talbutal	0.41	morphine	1.05
acetylated acetaminophen	0.43	hydrocodone	1.05
meconin	0.43	hydromorphone	1.07

pentobarbital	0.43	O^6 acetylmorphine	1.11
meperidine	0.45	acetylcodeine	1.12
secobarbital	0.46	thebaine	1.12
caffeine	0.48	O^3 acetylmorphine	1.13
antipyrine	0.52	oxycodone	1.13
diphenhydramine	0.53	acetyl thebol	1.14
lidocaine	0.54	chloroquine	1.24
aminopyrine	0.56	heroin	1.25
doxylamine	0.57	fentanyl	1.37
theophylline	0.57	quinine	1.48
phenobarbital	0.58	papaverine	1.50
dipyrone	0.62	strychnine	2.22
eicosane	0.63	noscapine	2.28

Method OPI-GCS

Instrument: Gas Chromatograph operated in split mode with FID

Column: 5% phenyl/95% methyl silicone 12 m x 0. 2mm x 0.33 µm film thickness

Carrier gas: Helium at 1.0 mL/min

Temperatures: Injector: 270°C
Detector: 280°C
Oven program:
1) 175°C initial temperature for 1.0 min
2) Ramp to 275°C at 15°C/min
3) Hold final temperature for 3.0 min

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

Samples are to be dissolved in 4:1 chloroform: methanol and filtered.

COMPOUND	RRT
tetracosane	0.95
codeine	**1.00 (6.13 min)**
morphine	1.03
thebaine	1.11
papaverine	1.36
noscapine	1.76
heroin	1.21

3.6. HIGH PERFORMANCE LIQUID CHROMATOGRAPHY

Method OPI-LCS1

Instrument: High performance liquid chromatograph equipped with diode array

Column: 5 µm ODS, 3.2 mm x 125 mm

Detector: UV, 210 nm, 228 nm and 240 nm

Flow: 0.76 mL/min

Injection Volume: 20 µL

Buffer: 3% 2 N sodium hydroxide and 1% phosphoric acid with 3 to 4.5 mL hexylamine added per 870 mL total buffer volume

Mobile Phase: Gradient:
Buffer: methanol 95:5 to equilibrate for 15 min
Buffer: methanol to 70:30 over 20 min and hold for 6 min
Buffer: methanol to 80:20 over 10 min and hold for 4 min
Buffer: methanol to 95:5 over 5 min

Samples are to be dissolved in 89:10:1 water: acetonitrile: glacial acetic acid, adjusted to pH 3.7 with 2 N sodium hydroxide, then filtered with a 0.45-micron filter.

COMPOUND	RRT
morphine	0.36
procaine	0.67
codeine	**1.00 (7.10 min)**
thebaine	1.65
noscapine	1.90
papaverine	2.14

4. SEPARATION TECHNIQUES

To isolate the opium alkaloids from the plant material for qualitative GC work, at least 300 mg of opium is placed in a 100 mL volumetric and 50 mL methanol added. Boil the mixture for 20 minutes and cool to room temperature before diluting to mark. Pipette 2 mL into a 5 mL test tube and evaporate with nitrogen stream. Add 0.5 mL of Tri-Sil Z and heat for 30 minutes at 80^{o}C. Dilute with methylene chloride and inject on GC.

5. QUANTITATIVE PROCEDURES

5.1. HIGH PERFORMANCE LIQUID CHROMATOGRAPHY

Method OPI-LCQ1 (Signature analysis)

Internal Standard Stock Solution:
Procaine hydrochloride in 89:10:1 water: acetonitrile: glacial acetic acid, adjusted to pH 3.7 with 2 N sodium hydroxide.

Standard Solution Preparation:
Accurately weigh and prepare a standard solution of the desired opiate using the internal standard stock solution.

Sample Preparation:
Accurately weigh an amount of sample into a volumetric flask and dilute with internal standard stock solution. If necessary, dilute the sample so the final concentration of the desired opiate approximates the standard concentration or falls within the linear range. Filter sample with 0.45-micron filter.

Method OPI-LCS1

Instrument: High performance liquid chromatograph equipped with diode array

Column: 5 µm ODS, 3.2 mm x 125 mm

Detector: UV, 210 nm, 228 nm and 240 nm

Flow: 0.76 mL/min

Injection Volume: 20 µL

Buffer: 3% 2 N sodium hydroxide and 1% phosphoric acid with 3 to 4.5 mL hexylamine added per 870 mL total buffer volume

Mobile Phase: Gradient:
Buffer: methanol 95:5 to equilibrate for 15 min
Buffer: methanol to 70:30 over 20 min and hold for 6 min
Buffer: methanol to 80:20 over 10 min and hold for 4 min
Buffer: methanol to 95:5 over 5 min

COMPOUND	RRT
morphine	0.36
procaine	0.67
codeine	**1.00 (7.10 min)**
thebaine	1.65
noscapine	1.90
papaverine	2.14

6. QUALITATIVE DATA
See spectra on the following pages for FT-IR, Mass Spectrometry, and Nuclear Magnetic Resonance.

7. REFERENCES

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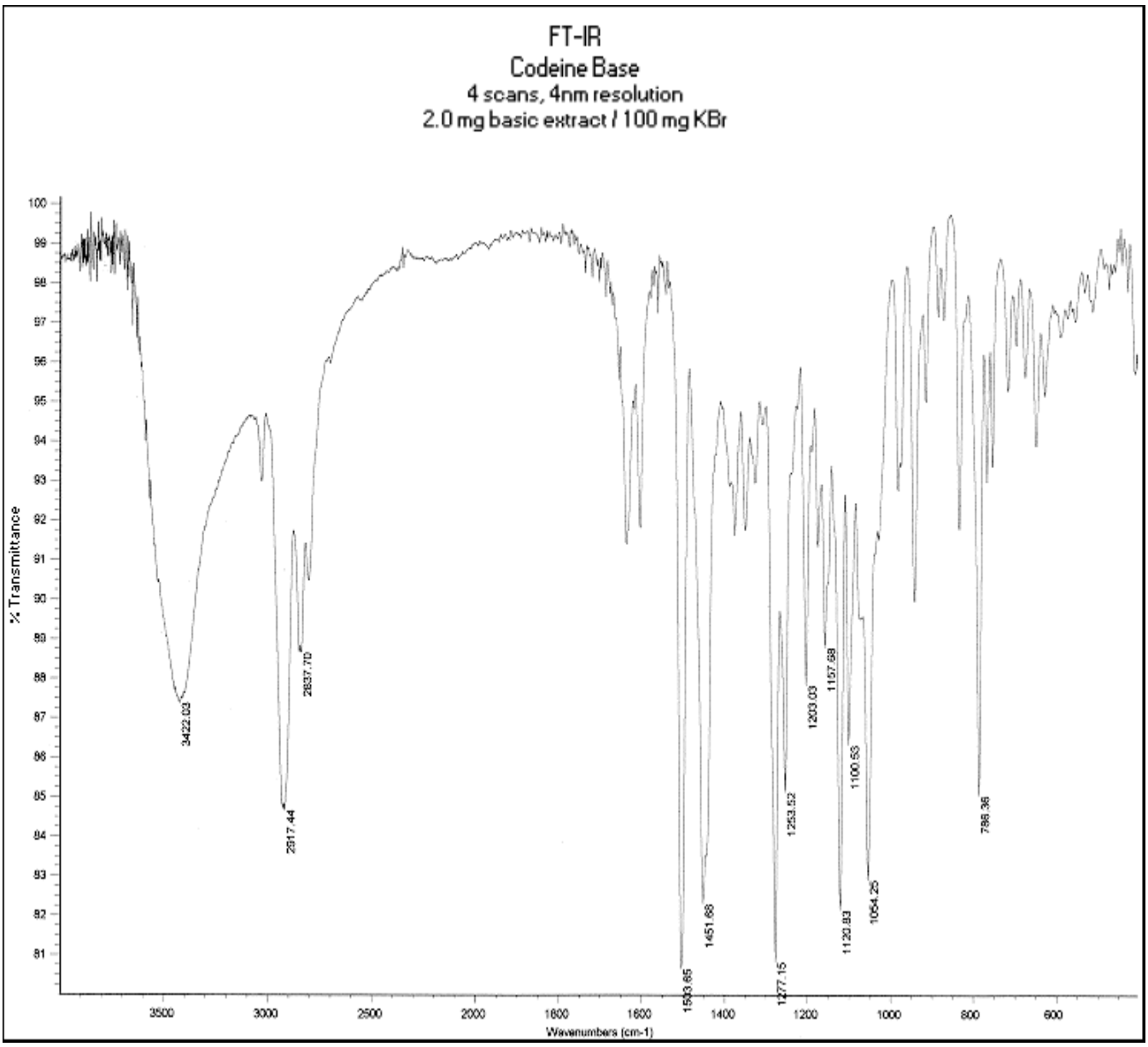
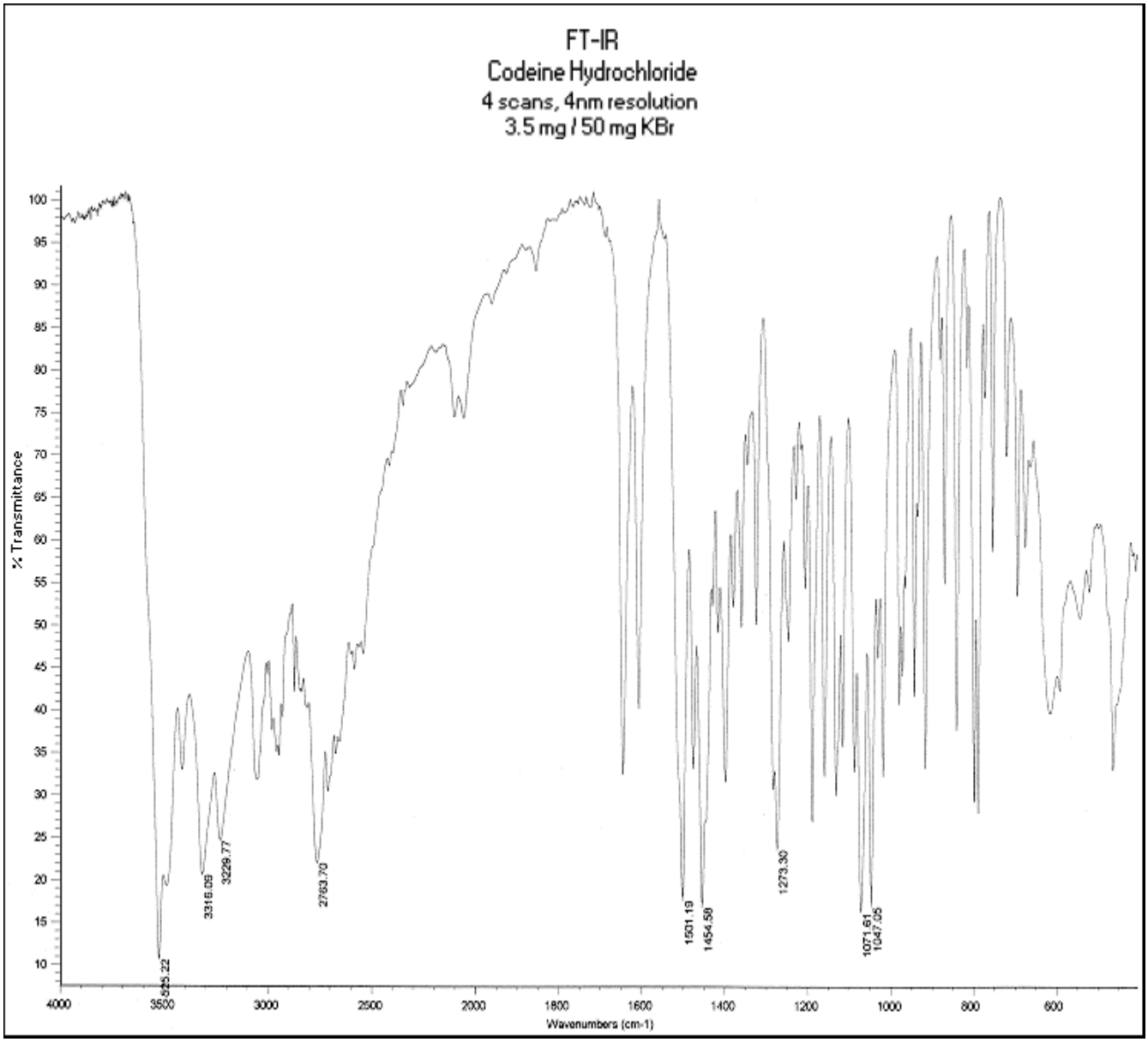
8. ADDITIONAL RESOURCES

Forendex

Wikipedia


FT-IR
Codeine Base
4 scans, 4nm resolution
2.0 mg basic extract / 100 mg KBr
% Transmittance
Wavenumbers (cm-1)
3422.03
2917.44
2837.70
1633.65
1451.68
1277.15
1253.52
1203.03
1157.68
1120.83
1100.53
1054.25
788.36


FT-IR
Codeine Hydrochloride
4 scans, 4nm resolution
3.5 mg / 50 mg KBr
% Transmittance
Wavenumbers (cm-1)
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3229.77
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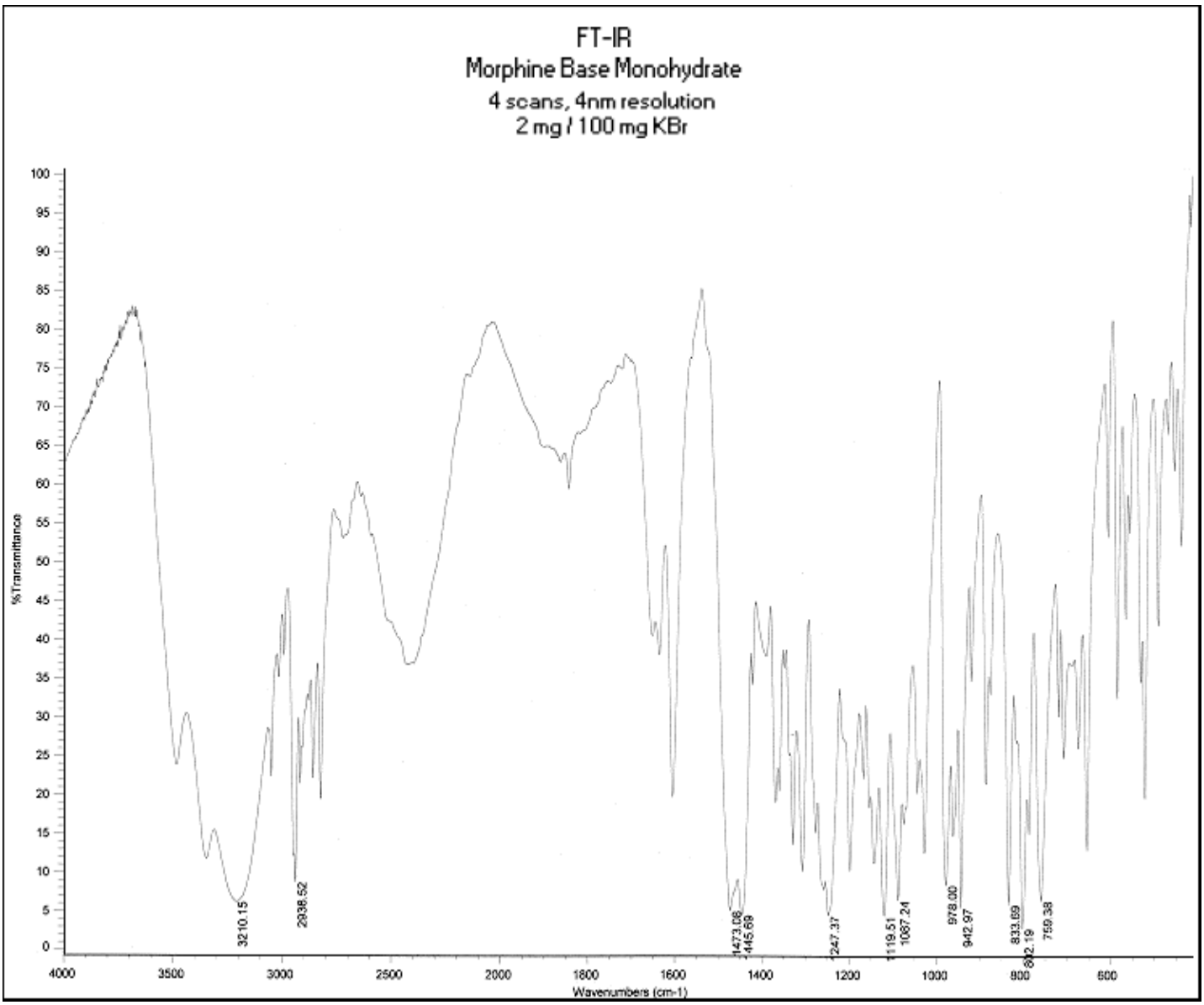
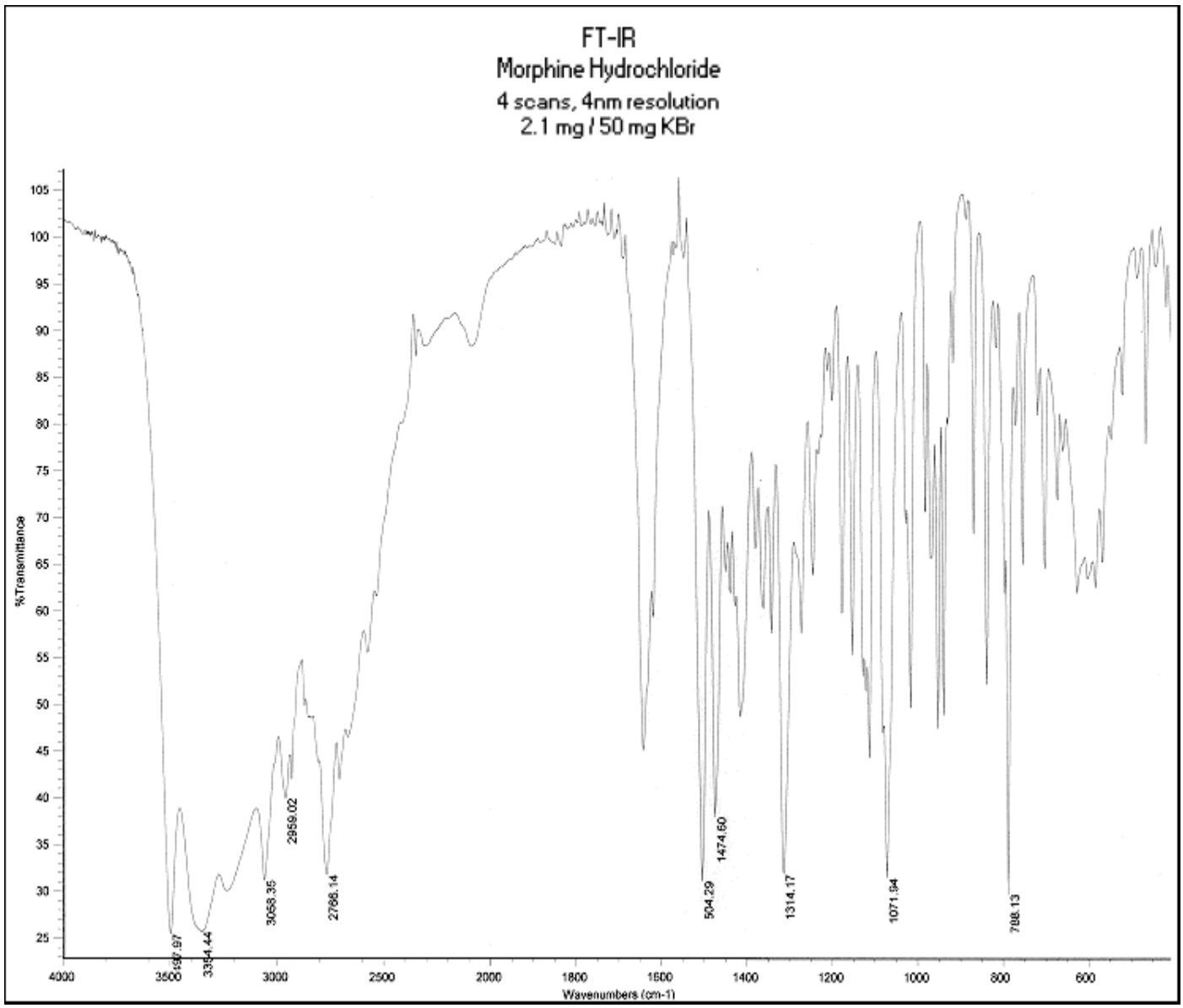
1631.19
1454.58
1273.30
1071.61
1047.05


FT-IR
Morphine Base Monohydrate
4 scans, 4nm resolution
2 mg / 100 mg KBr
%Transmittance
Wavenumbers (cm-1)
3210.15
2938.52
1473.08
1445.69
1247.37
1119.51
1067.24
978.00
942.97
833.69
802.19
759.38


FT-IR
Morphine Hydrochloride
4 scans, 4nm resolution
2.1 mg / 50 mg KBr
%Transmittance
Wavenumbers (cm-1)
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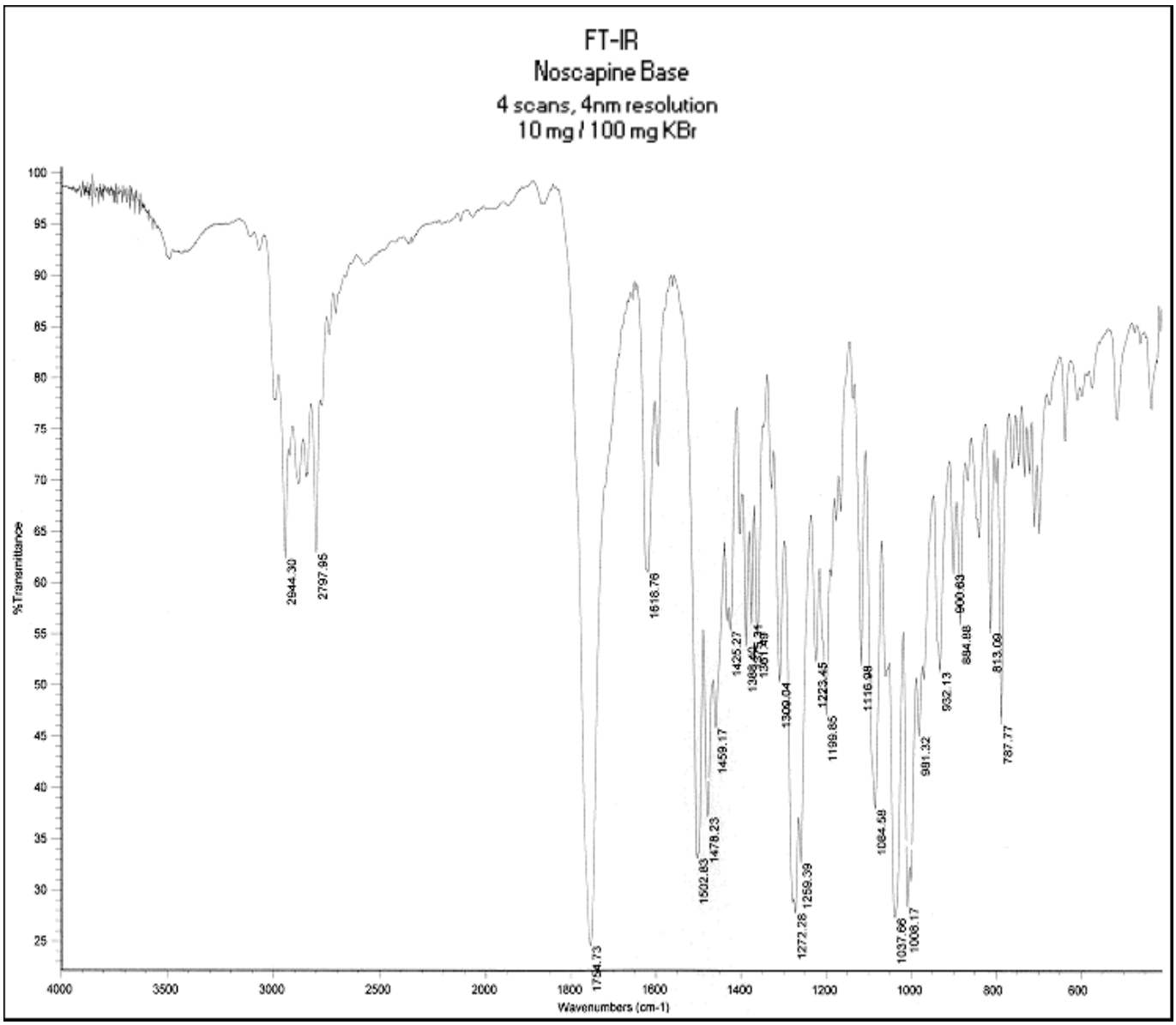
2959.02
2766.14
1474.60
1314.17
1071.94
788.13


FT-IR
Noscapine Base
4 scans, 4nm resolution
10 mg / 100 mg KBr
%Transmittance
Wavenumbers (cm-1)
2944.30
2797.95
1754.73
1616.76
1502.83
1478.23
1459.17
1425.27
1309.04
1272.28
1259.39
1223.45
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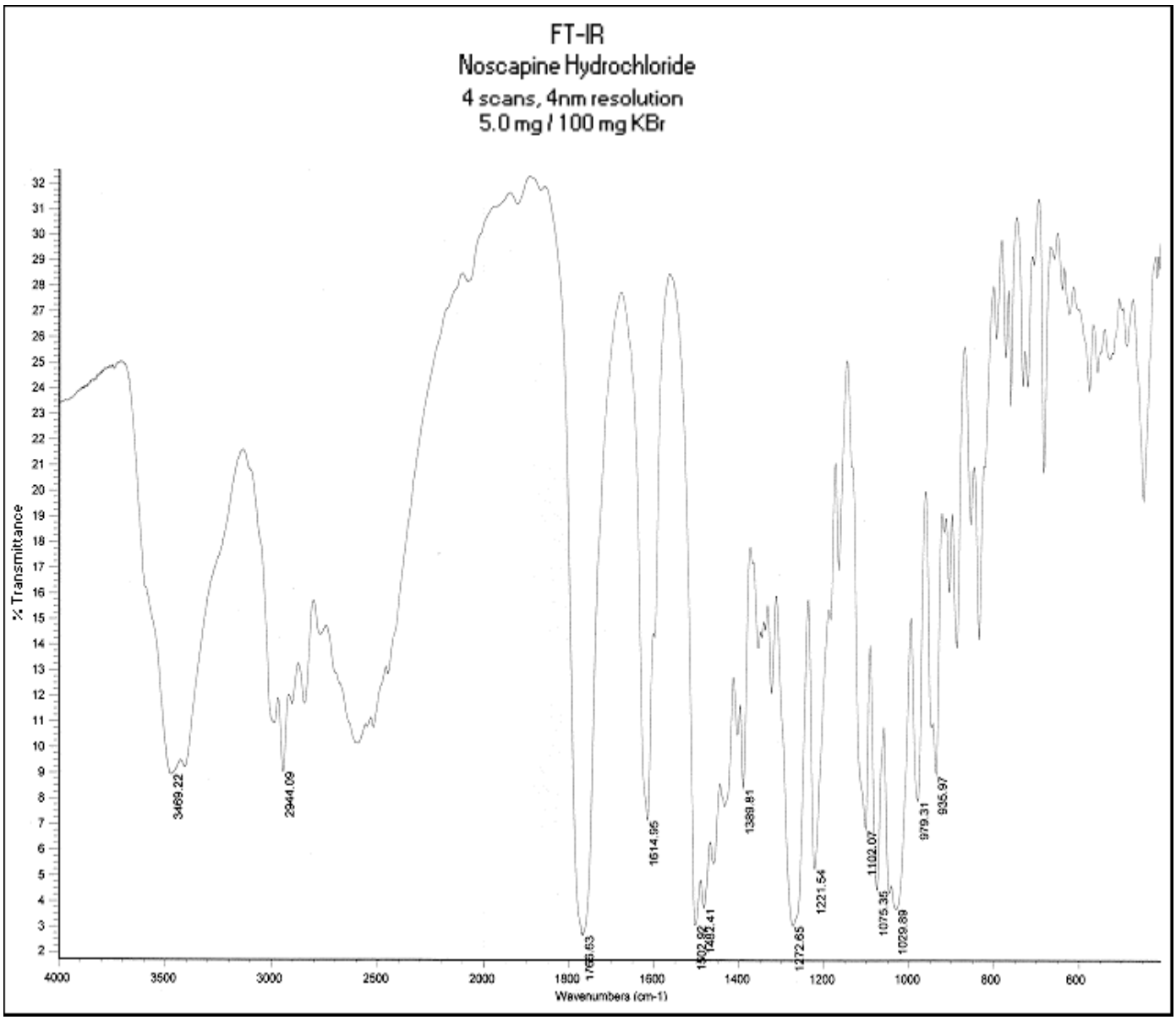
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5.0 mg / 100 mg KBr
% Transmittance
Wavenumbers (cm-1)
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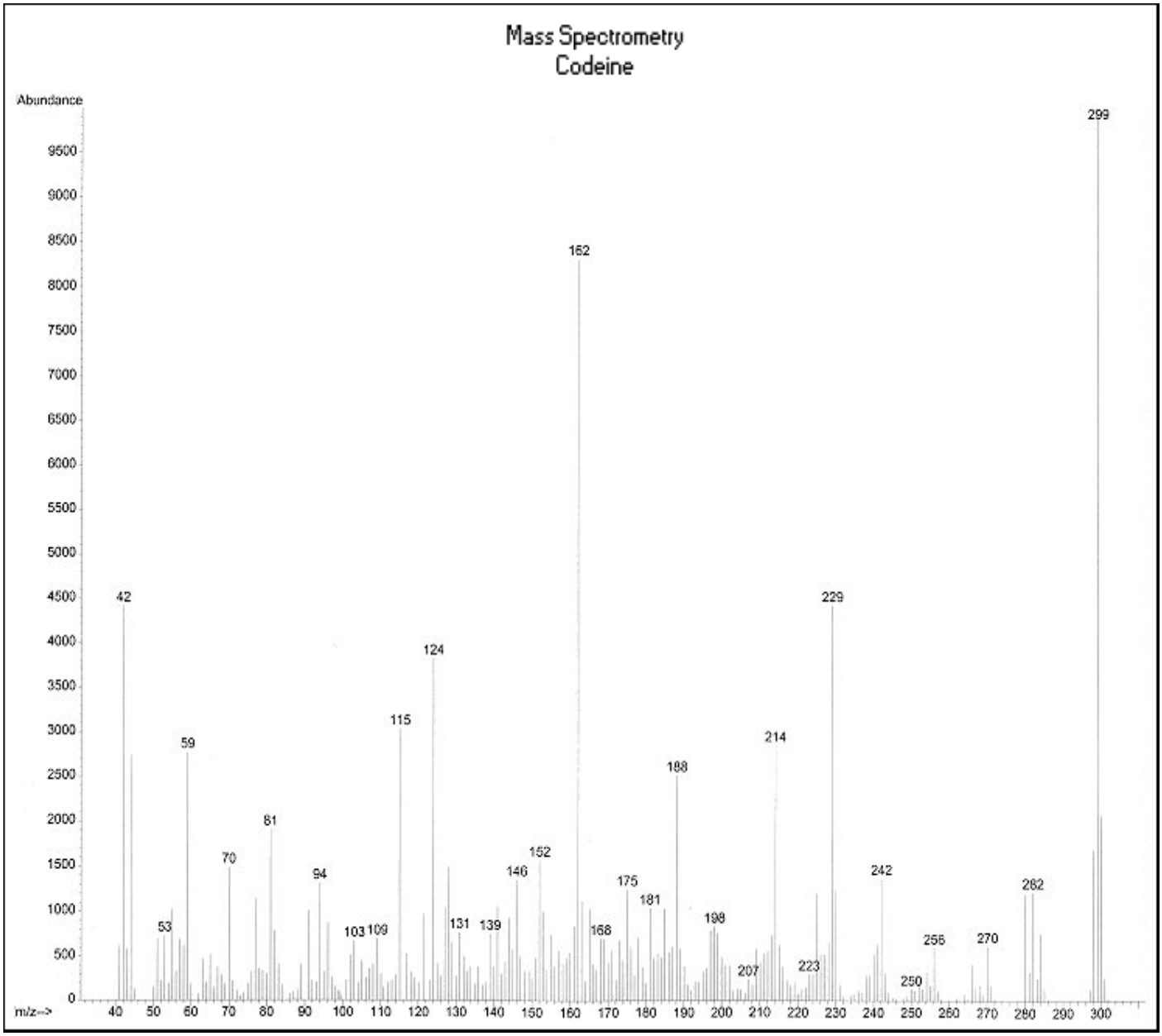
935.97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Codeine
Abundance
m/z-->
299
162
42
229
124
115
59
214
188
81
70
152
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103
109
131
139
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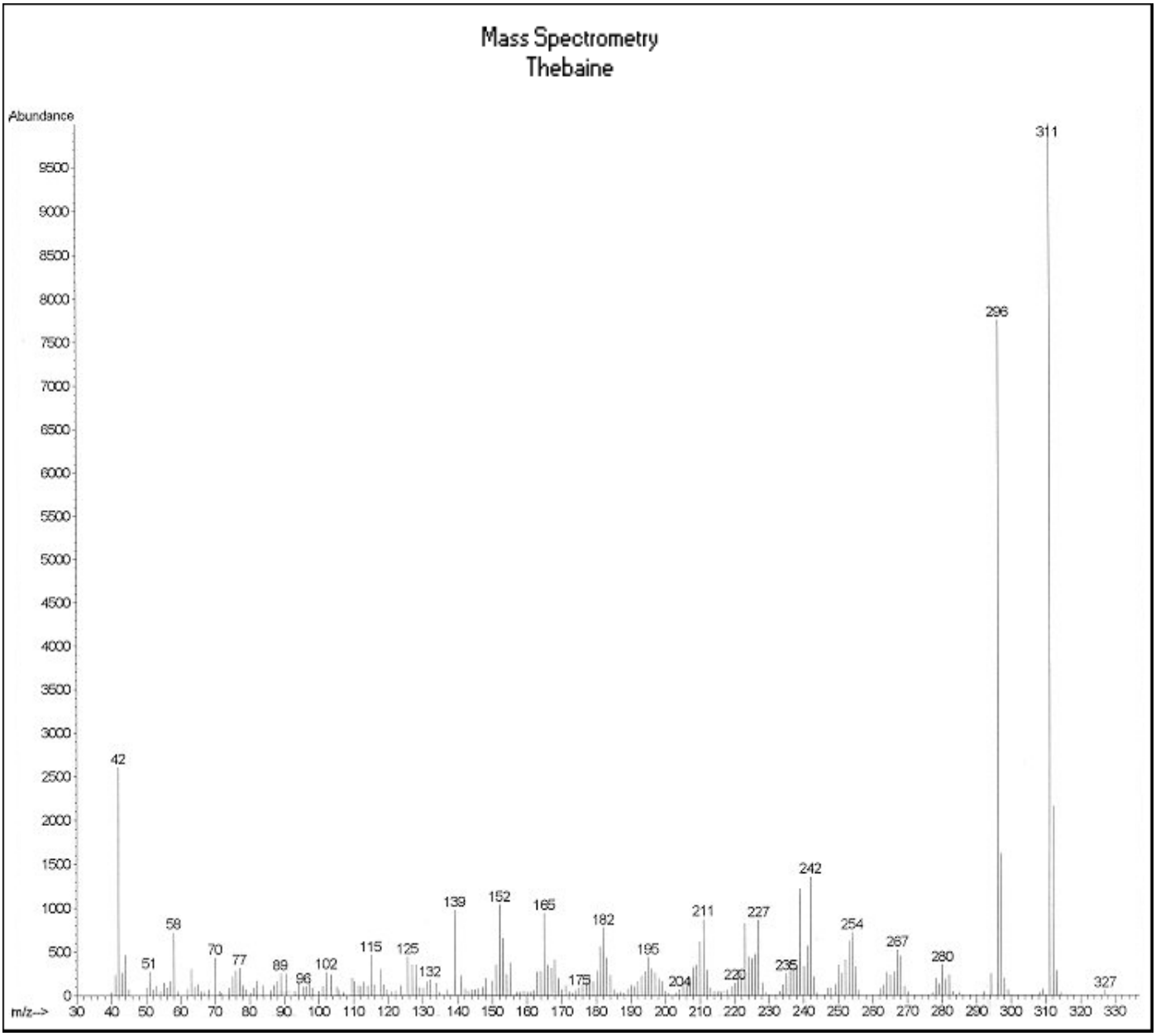
207
223
250
256
270


Mass Spectrometry
Thebaine
Abundance
m/z-->
311
296
42
58
70
77
89
96
102
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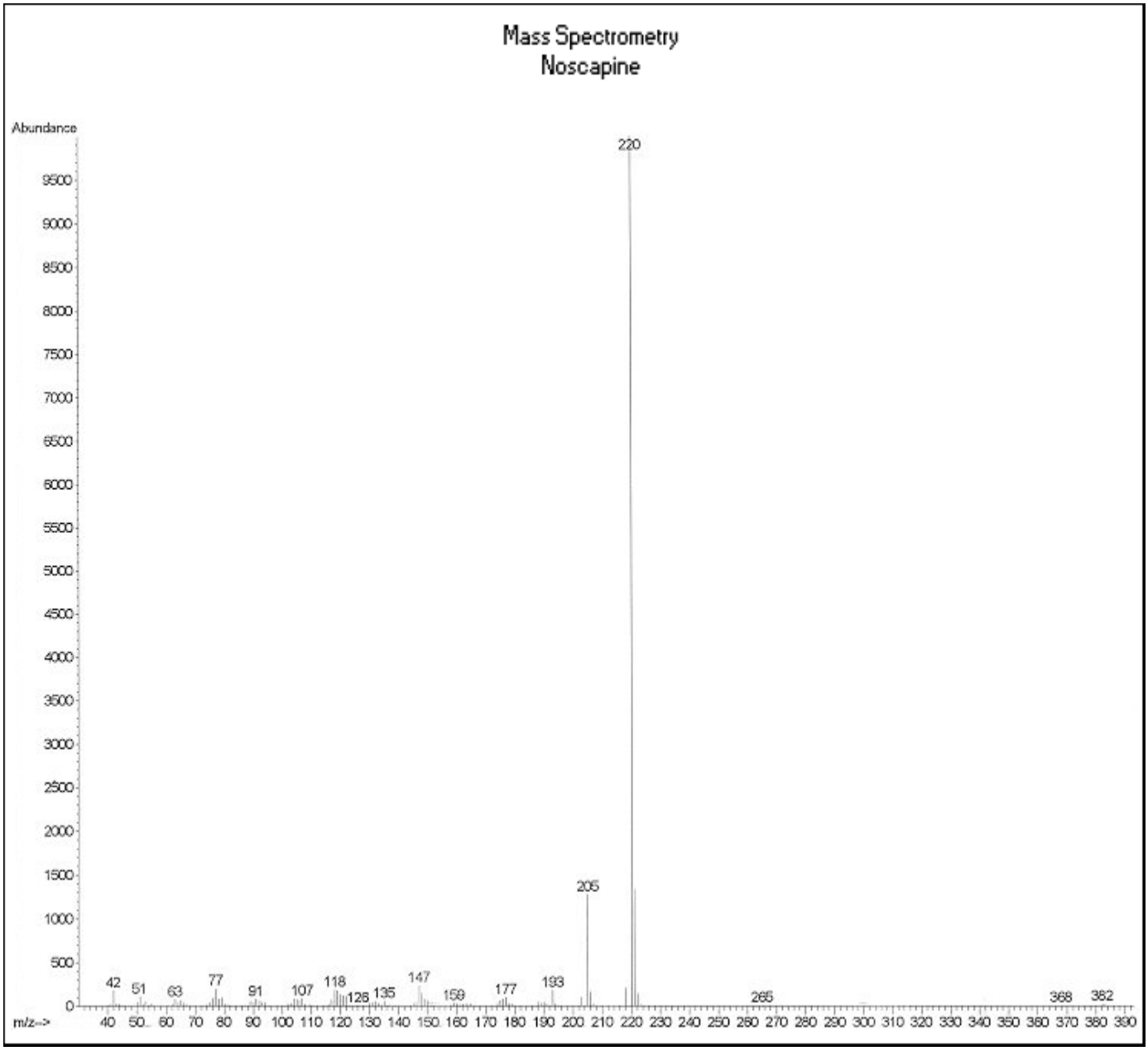
Mass Spectrometry
Noscapine
Abundance
m/z-->
220
205
42
51
63
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91
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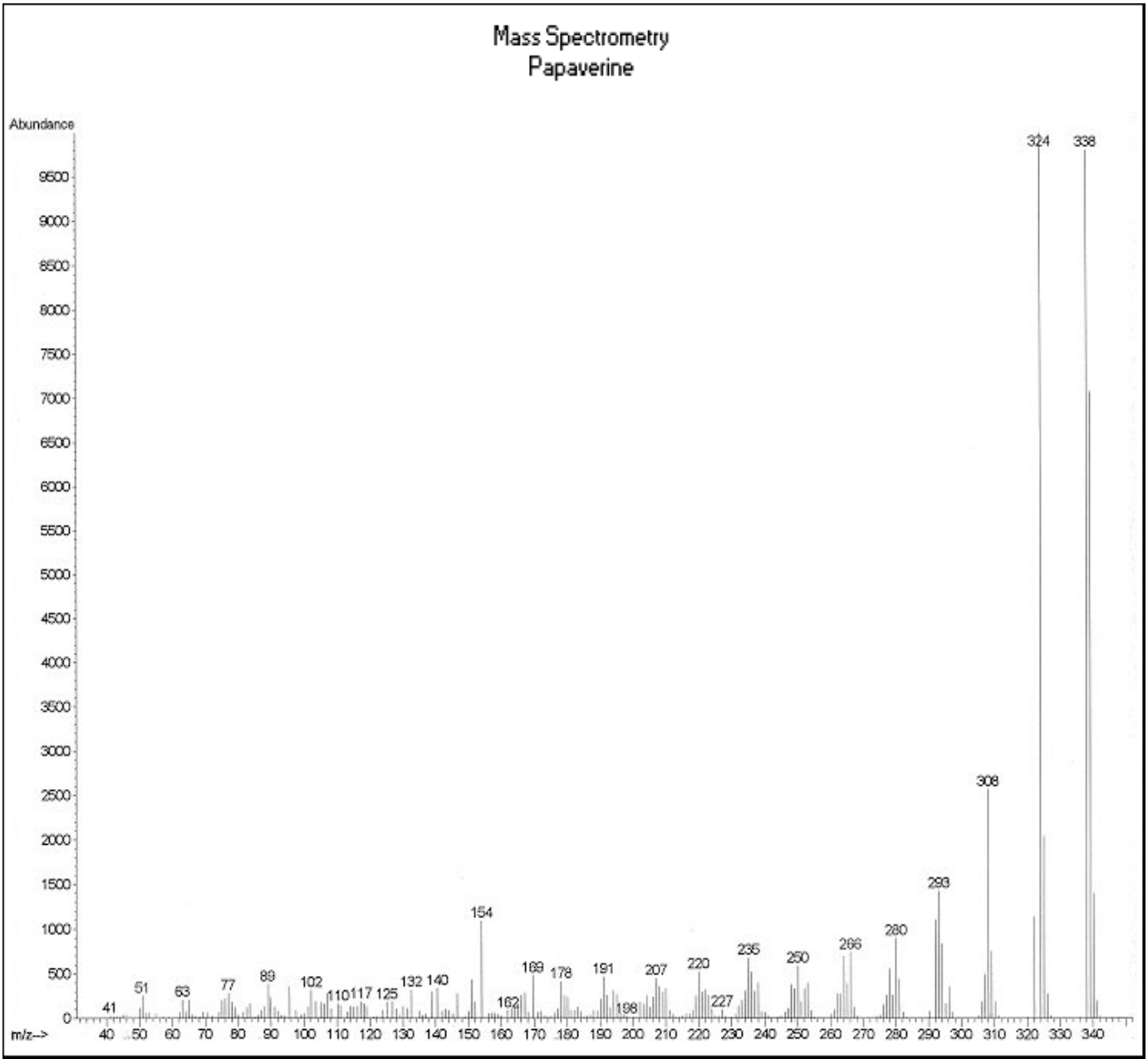
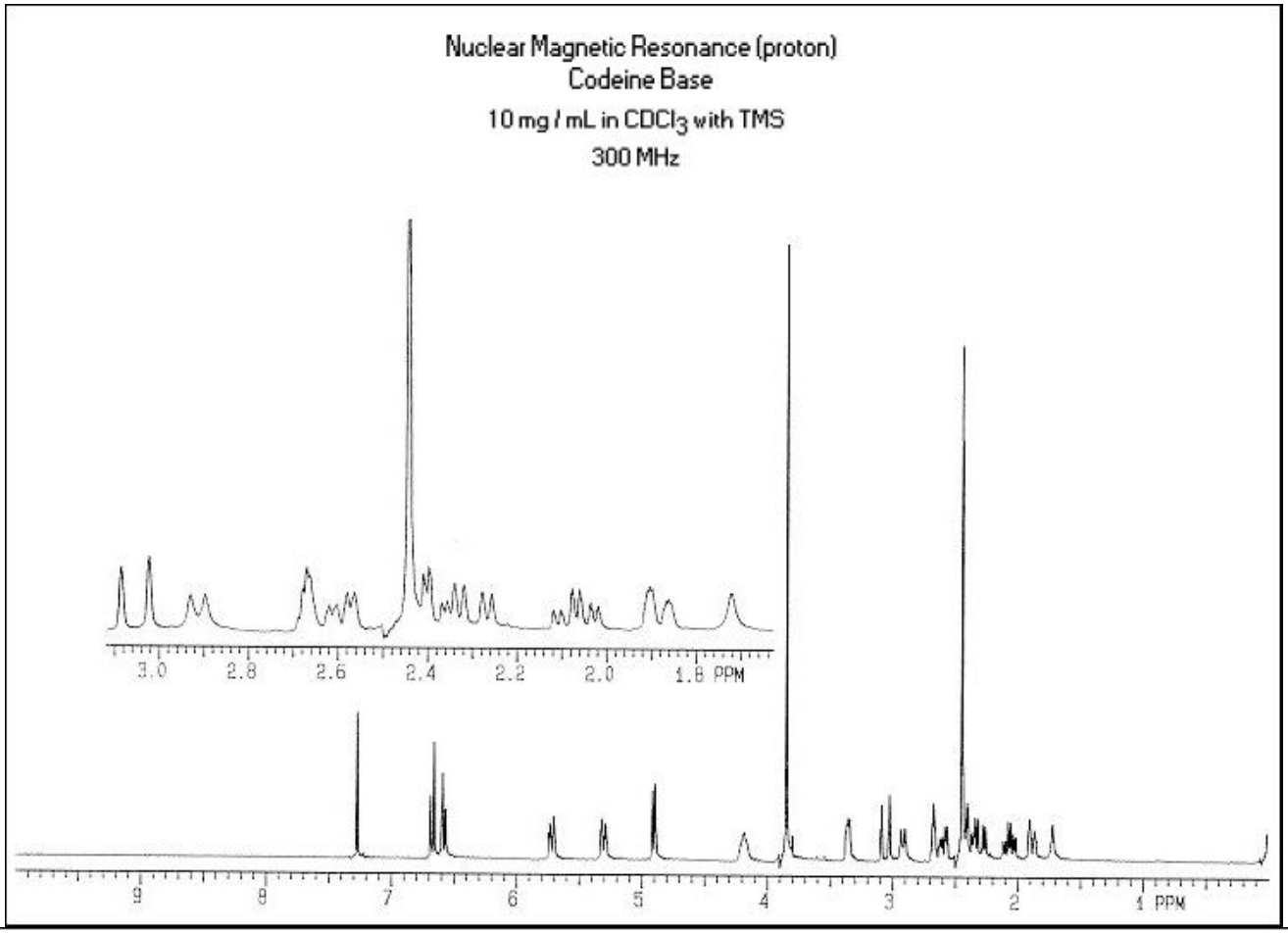
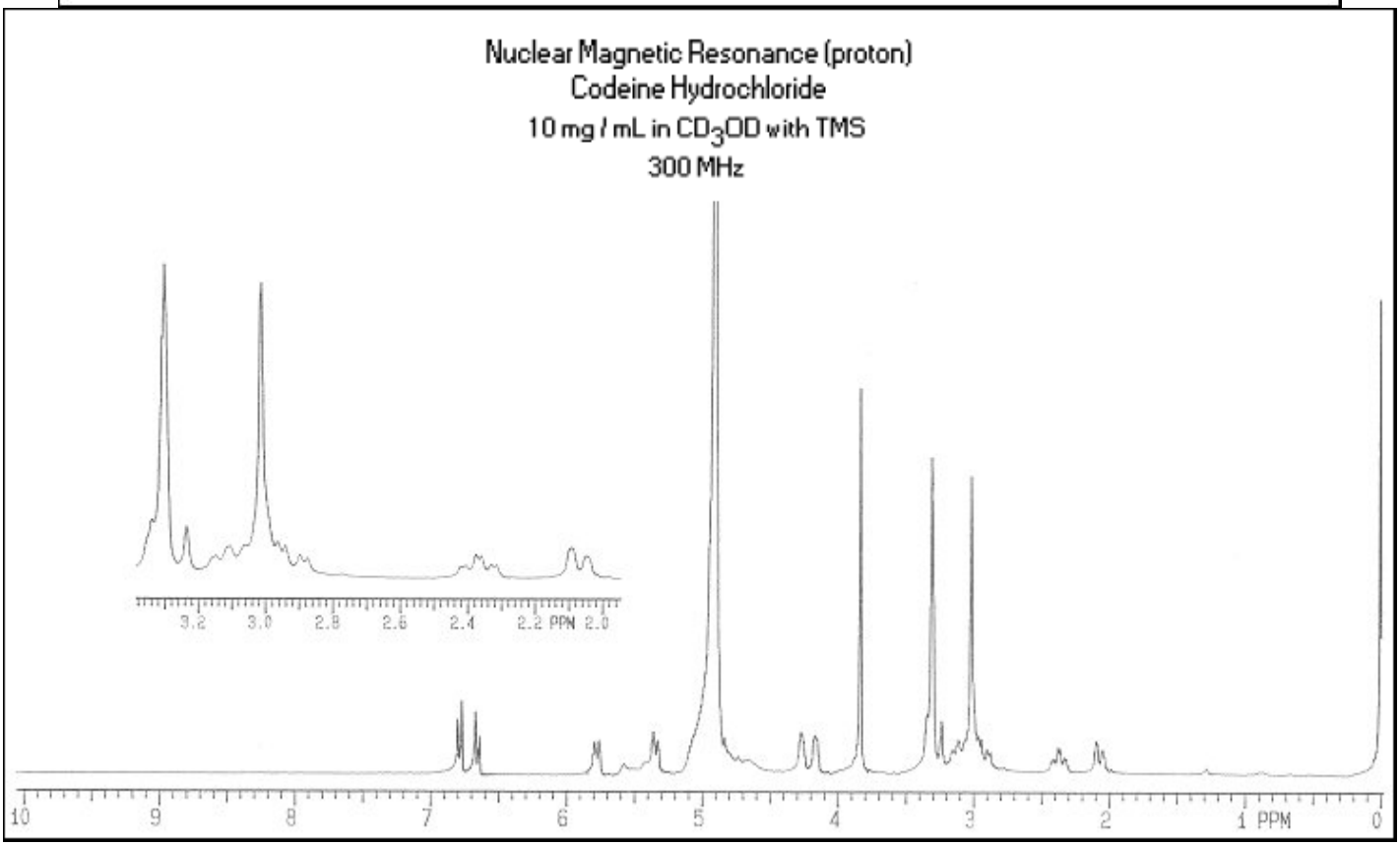

Mass Spectrometry
Papaverine
Abundance
m/z-->

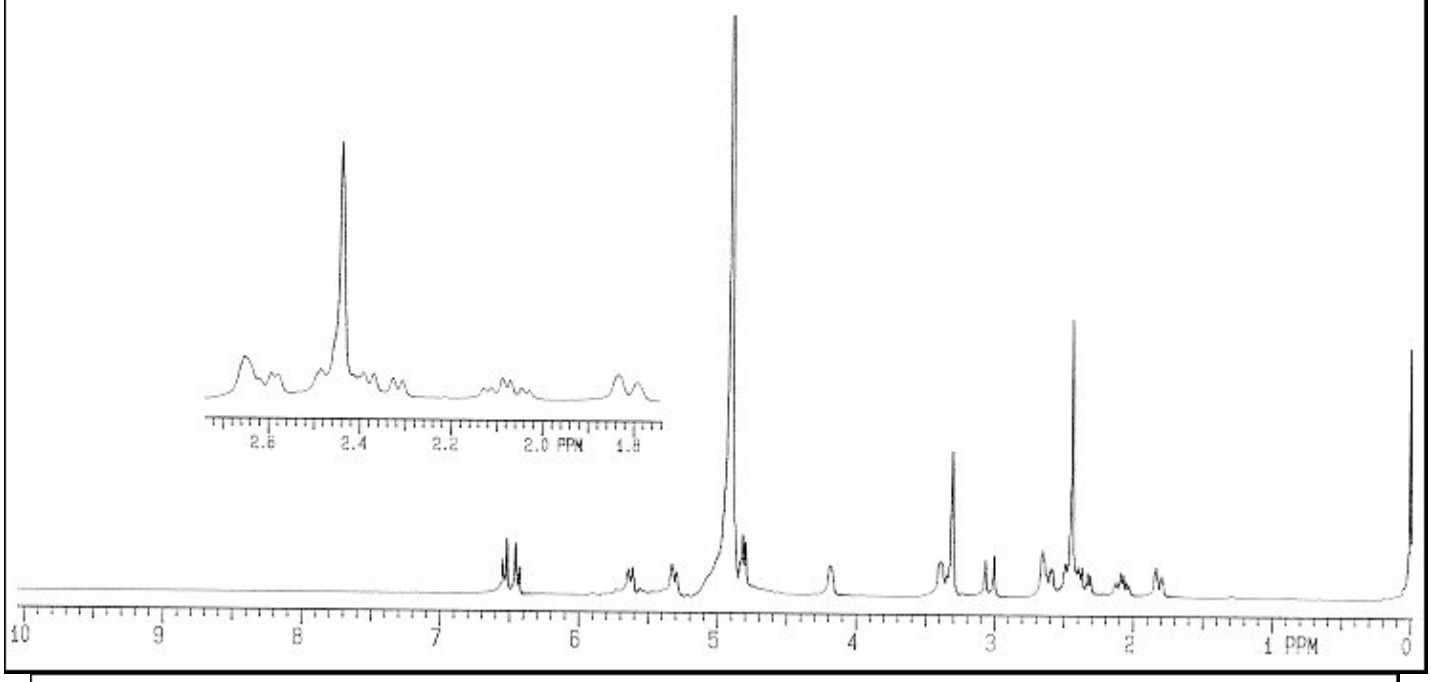
Nuclear Magnetic Resonance (proton)
Codeine Base
10 mg / mL in $CDCl_3$ with TMS
300 MHz



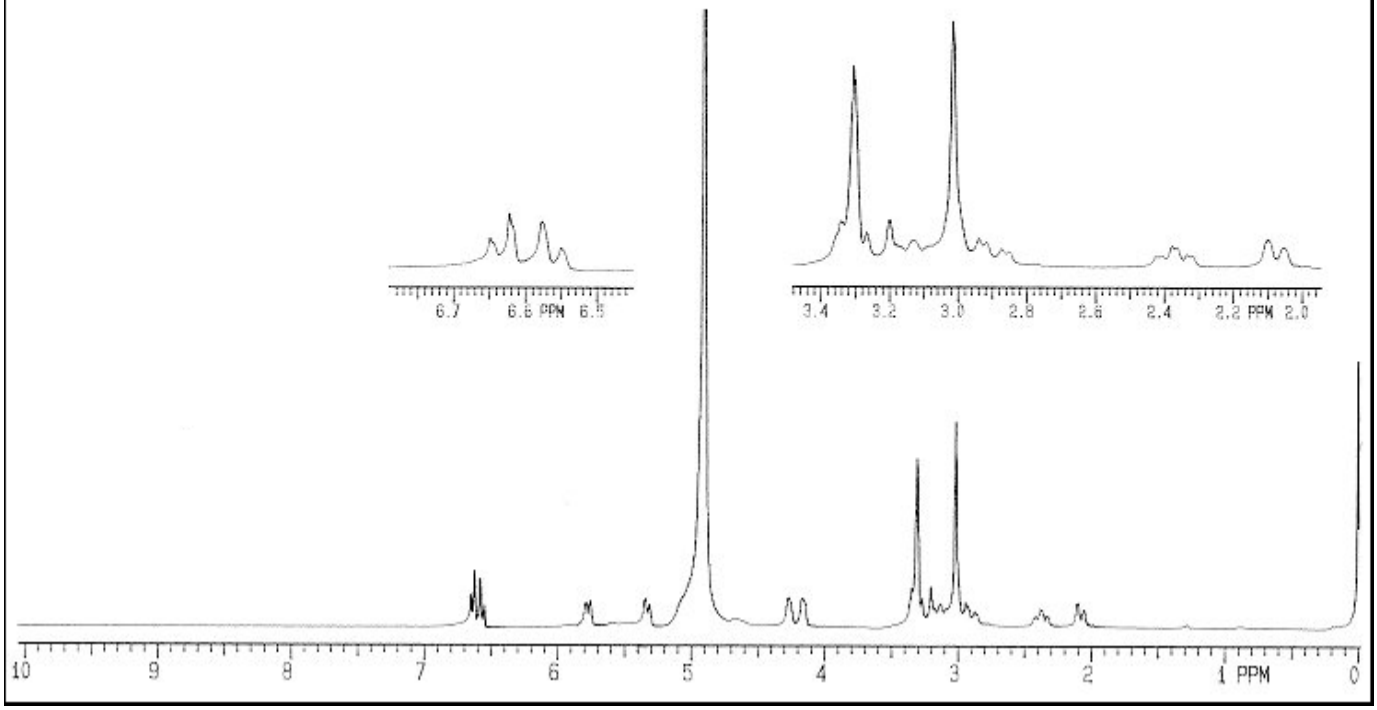
Nuclear Magnetic Resonance (proton)
Codeine Hydrochloride
10 mg / mL in CD_3OD with TMS
300 MHz



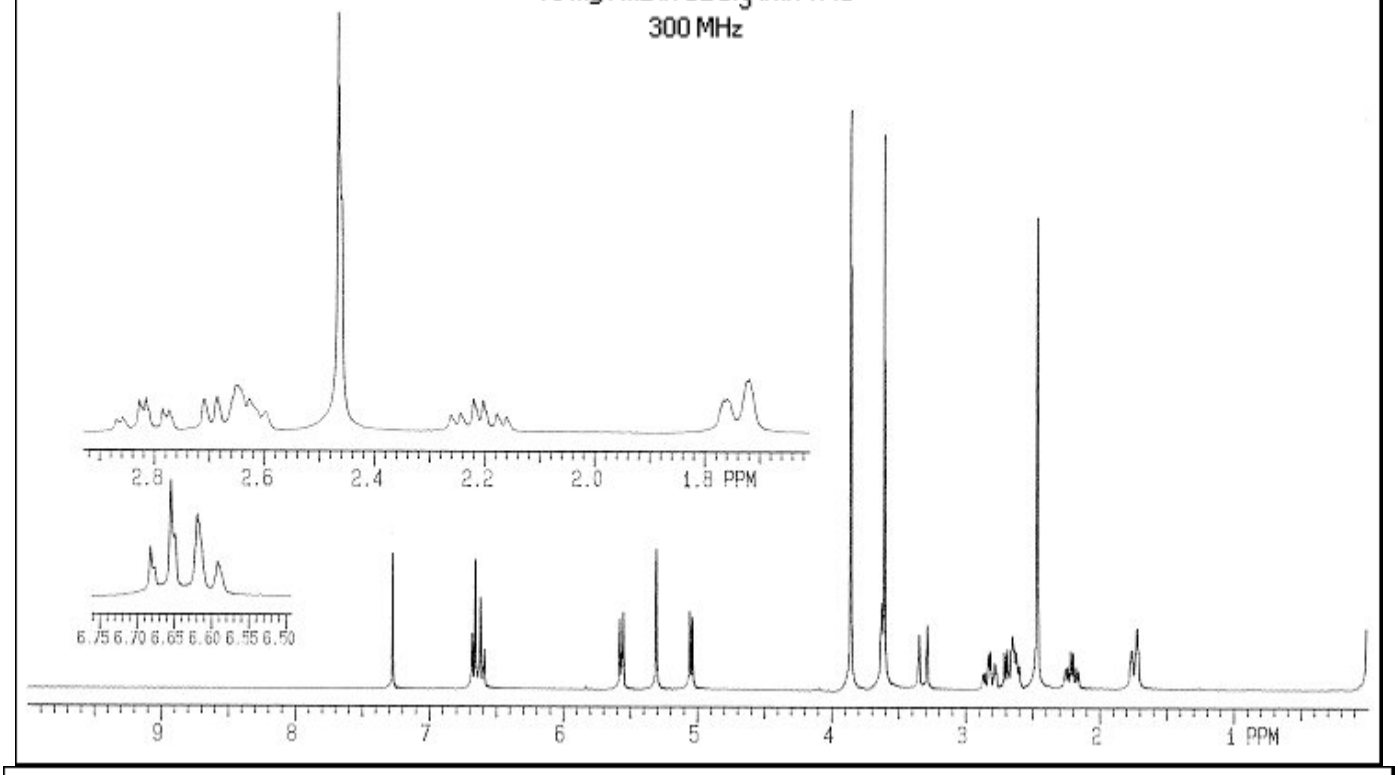
Nuclear Magnetic Resonance (proton)
Morphine Base Monohydrate
10 mg / mL in CD_3OD with TMS
300 MHz



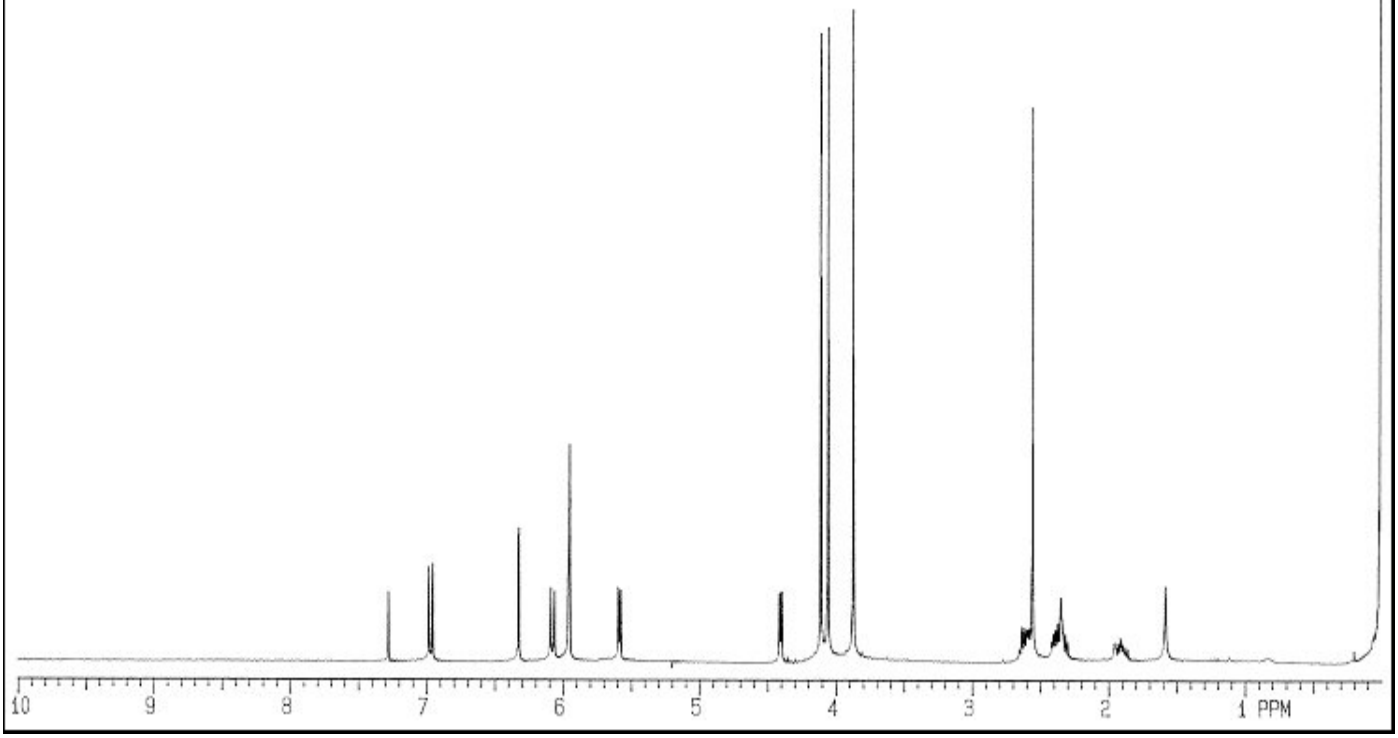
Nuclear Magnetic Resonance (proton)
Morphine Hydrochloride
10 mg / mL in CD_3OD with TMS
300 MHz

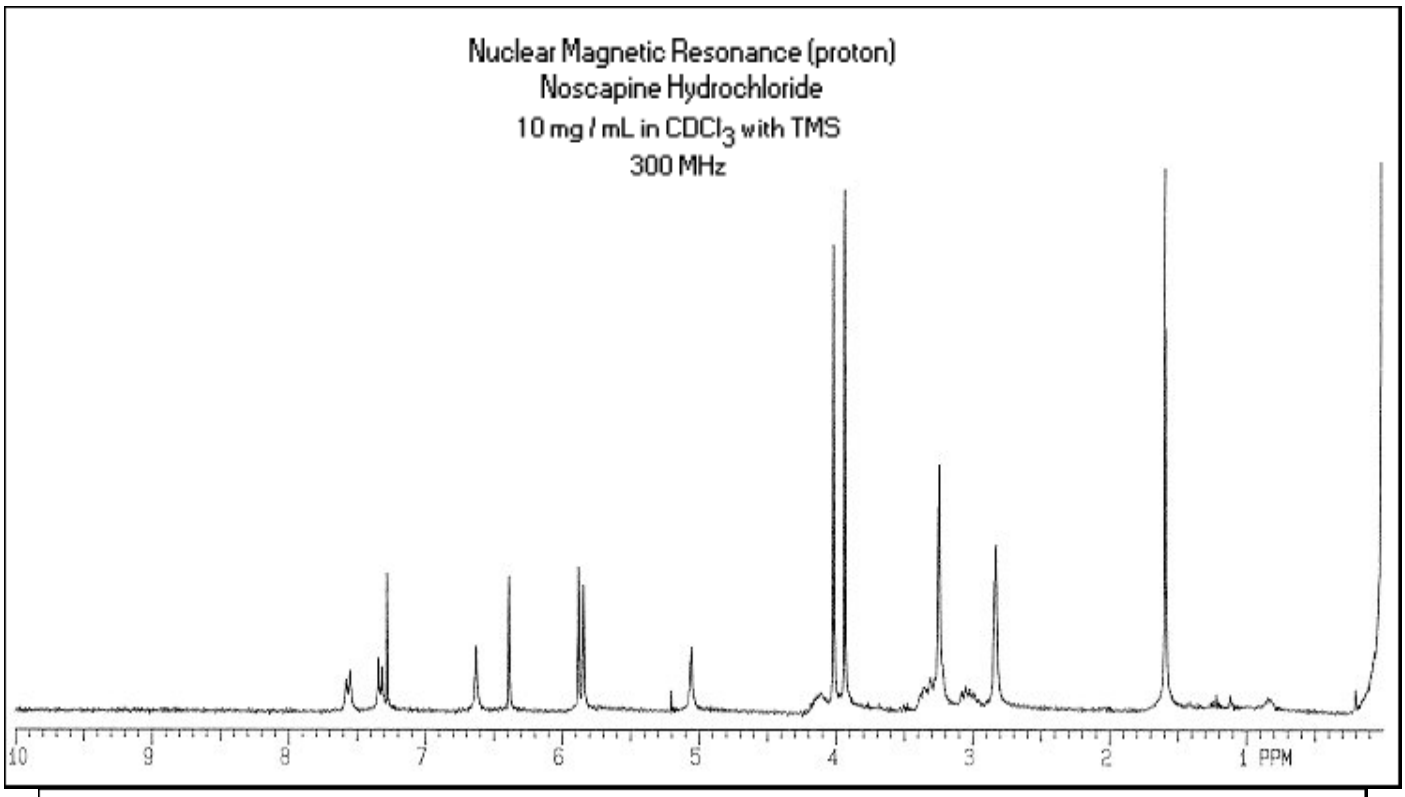


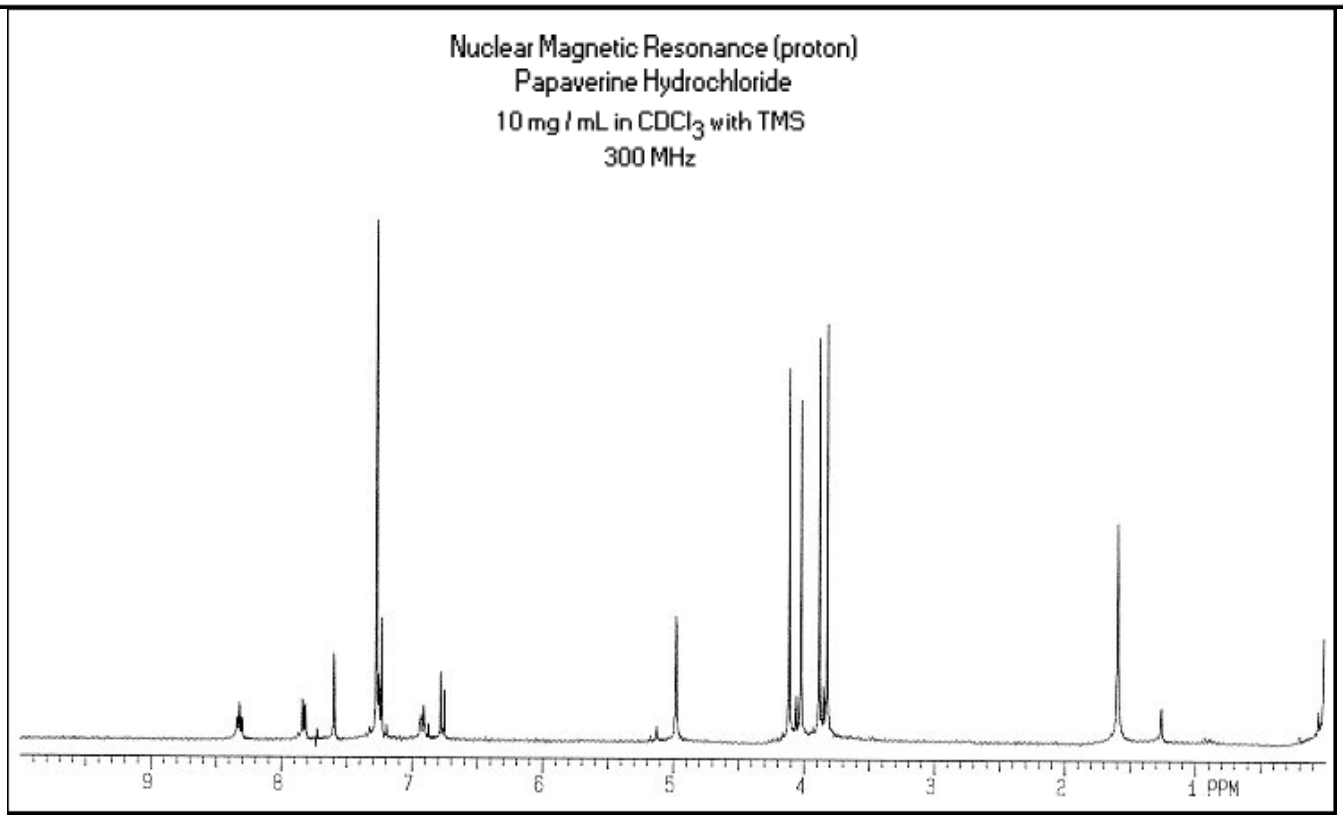
Nuclear Magnetic Resonance (proton)
Thebaine Hydrochloride
10 mg / mL in $CDCl_3$ with TMS
300 MHz



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




Nuclear Magnetic Resonance (proton)
Noscapine Hydrochloride
10 mg / mL in CDCl3 with TMS
300 MHz
10
9
8
7
6
5
4
3
2
1 PPM


Nuclear Magnetic Resonance (proton)
Papaverine Hydrochloride
10 mg / mL in CDCl3 with TMS
300 MHz
9
8
7
6
5
4
3
2
1 PPM