

### 1. SYNONYMS

<b>CFR:</b>	Diazepam
<b>CAS #:</b>	439-14-5
<b>Other Names:</b>	Alupram Apozepam Atensine Diacopin Dialar Diazemuls Dipam D-Tran Ducene E-Pam Evacalm Lorinin Methyldiazepinone Meval Neo-calme Novodipam Paxel Pro-pam Q-pam Sedapam Solis <b>Stesolid</b> Stress-pam Tensium Tranquase Valium

Valrelease  
 Vivol  
 7-Chloro-1,3-dihydro-1-methyl-5-phenyl-2H-1, 4-benzodiazepin-2-one

## 2. CHEMICAL AND PHYSICAL DATA

### 2.1. CHEMICAL DATA

Form	Chemical Formula	Molecular Weight	Melting Point (°C)
Diazepam	C <sub>16</sub> H <sub>13</sub> ClN <sub>2</sub> O	284.7	131-135

### 2.2. SOLUBILITY

Form	A	C	E	H	M	W
Diazepam	FS	FS	PS	PS	S	SS

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
Wagner's	Brown, brown-black precipitate, brown solution
Janovsky	Violet

### 3.2. THIN LAYER CHROMATOGRAPHY

#### Visualization

Acidified iodoplatinate spray

COMPOUND	RELATIVE R <sub>1</sub> and COLOR	
	System TLC 11	System TLC7

cocaine	0.8, purple	0.7, reddish
<b>diazepam</b>	1.0, red	1.0, reddish
flunitrazepam	1.0, light pink	1.0, reddish

### 3.3. GAS CHROMATOGRAPHY

#### *Method DIA-GCSI*

<b>Instrument:</b>	Gas chromatograph operated in split mode with FID
<b>Column:</b>	100% dimethylpolysiloxane 30 m x 0.25 mm x 0.25 µm
<b>Carrier gas:</b>	Hydrogen at 1.9 mL/min
<b>Temperatures:</b>	Injector: 265°C Detector: 285°C Oven program: 1) 120°C initial temperature for 1.0 min 2) Ramp to 270°C at 15°C/min 3) Hold final temperature for 4.0 min
<b>Injection Parameters:</b>	Split Ratio = 25:1, 1 µL injected

Samples are to be dissolved in methylene chloride and filtered.

COMPOUND	RRT	COMPOUND	RRT
ephedrine	0.24	dextropropoxyphene	0.86
MDA	0.31	codeine	0.96
aspirin	0.32	morphine	0.99
MDMA	0.36	<b>diazepam</b>	<b>1.00 (11.65 min)</b>
guaifenesin	0.44	tetracosane	1.00
meprobamate	0.56	thorazine	1.04
methapyrilene	0.71	flunitrazepam	1.10
methocarbomal	0.73	heroin	1.11

cocaine	0.85		
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### 3.4. HIGH PERFORMANCE LIQUID CHROMATOGRAPHY

#### *Method DIA-LCSI*

<b>Instrument:</b>	High performance liquid chromatograph equipped with diode array
<b>Column:</b>	5 µm ODS, 150 mm x 3.2 mm
<b>Detector:</b>	UV, 210 nm
<b>Flow:</b>	1.0 mL/min
<b>Injection Volume:</b>	3.0 µL
<b>Buffer:</b>	4000 mL distilled water, 22.5 mL phosphoric acid adjust to pH 2.3 with triethylamine
<b>Mobile Phase:</b>	Buffer: acetonitrile 50:50

Samples are to be dissolved in acetonitrile and filtered with a 0.45-micron filter.

COMPOUND	RRT	COMPOUND	RRT
flunitrazepam	0.73	<b>diazepam</b>	<b>1.00 (8.46)</b>

### 4. SEPARATION TECHNIQUES

Diazepam is most often distributed in tablet form and may be isolated from tablet material by chloroform, ether, or methanol solvent washes.

Diazepam has a dissociation constant ( $pK_a$ ) of 3.3, and may be extracted from an aqueous alkaline solution using organic solvents.

### 5. QUANTITATIVE PROCEDURES

#### 5.1. GAS CHROMATOGRAPHY

##### *Method DIA-GCQ1*

*Internal Standard Stock Solution:*

1.0 mg/mL docosane in methylene chloride.

*Standard Solution Preparation:*

Accurately weigh and prepare a standard solution of diazepam at approximately 1.0 mg/mL using above 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 approximates the standard concentration.

*Instrument:*

Gas chromatograph operated in split mode with FID

*Column:*

5% diphenyl/95% dimethyl polysiloxane 30 m x 0.53 mm x 0.50 µm film thickness

*Carrier gas:*

Hydrogen at 3.5 mL/min

*Temperatures:*

Injector: 265°C  
Detector: 285°C  
Oven program: 265°C isothermal

*Injection Parameters:*

Split Ratio = 25:1, 1 µL injected

*Typical Retention Time:*

Diazepam: 3.9 min  
Docosane: 2.2 min

*Linear Range:*

0.5 - 5.0 mg/mL

*Repeatability:*

RSD less than 0.3%

*Correlation Coefficient:*

0.999

*Accuracy:*

Error less than 5%

COMPOUND	RRT	COMPOUND	RRT
docosane	0.56	quazepam	1.03
cocaine	0.65	heroin	1.17
lorazepam	0.95	flunitrazepam	1.40
<b>Diazepam</b>	<b>1.00 (3.9 min)</b>	prazepam	1.50

## 5.2. CAPILLARY ELECTROPHORESIS

### *Method DIA-CEQ1*

#### *Internal Standard Stock Solution:*

0.2 mg/mL tetracaine in 1.0 N HCl.

#### *Standard Solution Preparation:*

Accurately weigh and prepare a standard solution of diazepam at approximately 0.3 mg/mL using above internal standard stock solution. Although diazepam is soluble in 1.0 N HCl, the solution should be made fresh to avoid possible breakdown of diazepam over time.

#### *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 approximates the standard concentration.

<b><i>Mode:</i></b>	Free zone
<b><i>Column:</i></b>	48.5 cm x 50 µm fused silica capillary
<b><i>Run Buffer:</i></b>	50 mM sodium phosphate buffer, pH 2.5
<b><i>Detector:</i></b>	UV, 210 nm
<b><i>Voltage:</i></b>	27 kV
<b><i>Temperature:</i></b>	25°C air cooled
<b><i>Injection:</i></b>	1 s hydrodynamic
<b><i>Run Time:</i></b>	12 min
<b><i>Rinse Time:</i></b>	2 min
<b><i>Linear Range:</i></b>	0.04 - 0.80 mg/mL
<b><i>Repeatability:</i></b>	RSD less than 3.0%
<b><i>Correlation Coefficient:</i></b>	0.999
<b><i>Accuracy:</i></b>	Error less than 5%

## QUALITATIVE DATA

### 6.1. ULTRAVIOLET SPECTROPHOTOMETRY

<b>Solvent</b>	<b>Maximum Absorbance (nm)</b>
Hydrochloric or sulfuric acid	242

## **6.2. INFRARED SPECTROSCOPY (FT-IR)**

An additional difficulty in comparing the IR spectra of diazepam arises from the existence of different crystalline forms or polymorphs which generate differences in spectra. To overcome this difficulty, both sample and standard should be subjected to the same preparations.

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

## **7. REFERENCES**

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

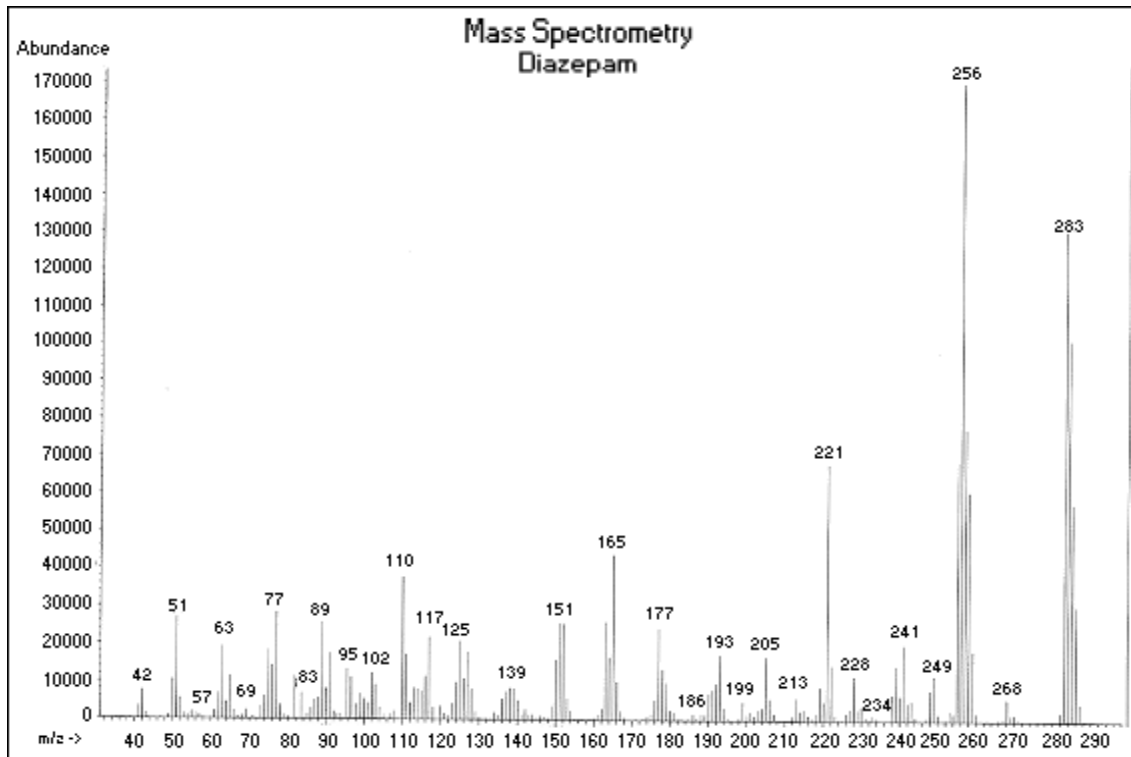
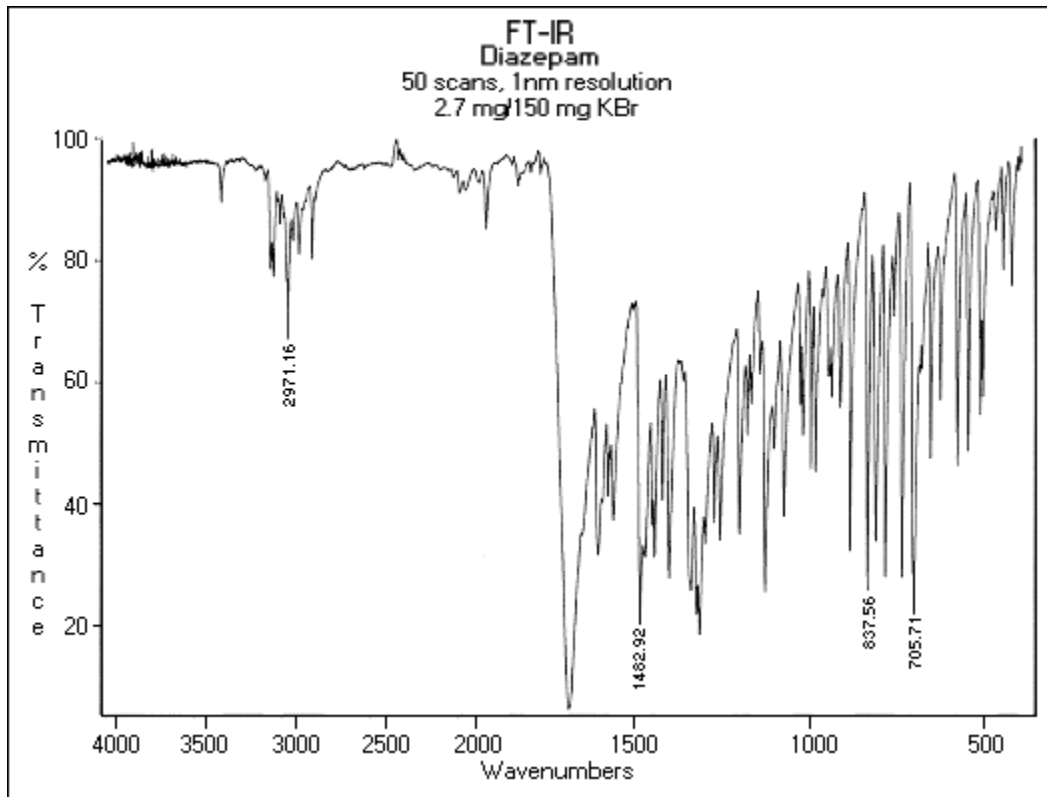
Budavari, S., *the Merck Index, 12<sup>th</sup> Edition*, Merck and Co., Inc., 1996, p. 508.

## **8. ADDITIONAL RESOURCES**

[Forendex](#)

[Wikipedia](#)

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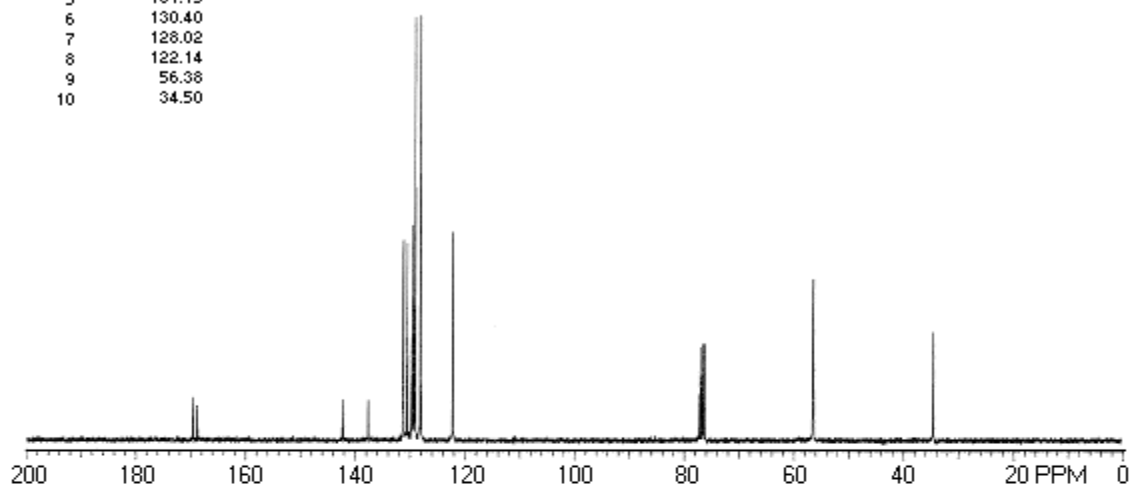


### Nuclear Magnetic Resonance (carbon)

Diazepam

50 mg/mL CDCL<sub>3</sub> with TMS  
75 MHz

PEAK	PPM
1	169.45
2	168.64
3	142.17
4	137.56
5	131.15
6	130.40
7	128.02
8	122.14
9	56.38
10	34.50

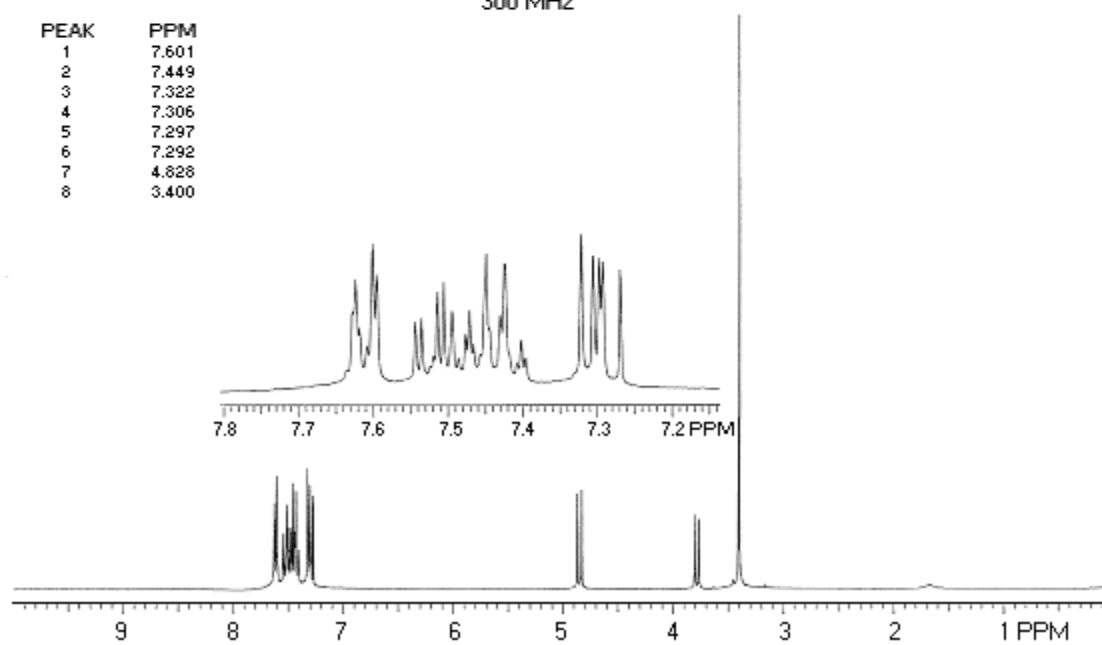


### Nuclear Magnetic Resonance (proton)

Diazepam

10 mg/mL CDCL<sub>3</sub> with TMS  
300 MHz

PEAK	PPM
1	7.601
2	7.449
3	7.322
4	7.306
5	7.297
6	7.292
7	4.828
8	3.400



Vapor Phase IR  
Diazepam  
0.8 mg/mL in CH<sub>3</sub>OH

