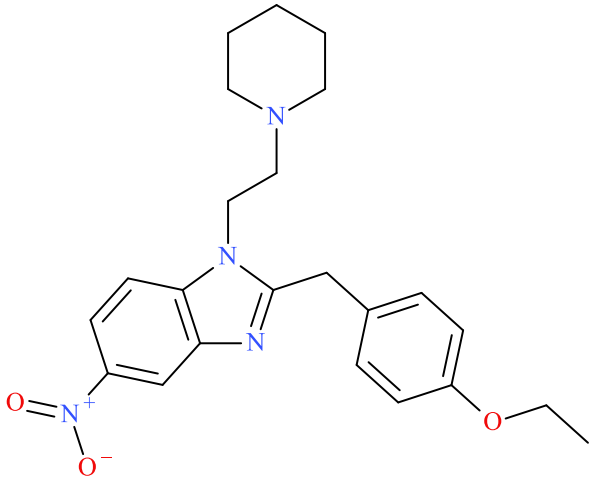
N-Piperidinyl Etonitazene

Sample Type: **Biological Sample**



Latest Revision: **November 22, 2021**

Date Received: **October 18, 2021**

Date of Report: **November 22, 2021**

1. GENERAL INFORMATION

IUPAC Name:	2-[(4-ethoxyphenyl)methyl]-5-nitro-1-[2-(1-piperidyl)ethyl]benzimidazole
InChI String:	InChI=1S/C23H28N4O3/c1-2-30-20-9-6-18(7-10-20)16-23-24-21-17-19(27(28)29)8-11-22(21)26(23)15-14-25-12-4-3-5-13-25/h6-11,17H,2-5,12-16H2,1H3
CFR:	Not Scheduled (11/2021)
CAS#	Not Available
Synonyms:	Etonitazepipne, *N*-Piperidyl Etonitazene
Source:	ACMT's Toxicology Investigators Consortium (ToxIC)

***Important Note**: All identifications were made based on evaluation of analytical data (LC-QTOF-MS) in comparison to analysis of acquired reference material.*

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2. CHEMICAL AND PHYSICAL DATA

2.1 CHEMICAL DATA

Drug	Chemical Formula	Molecular Weight	Molecular Ion $[M^+]$	Exact Mass $[M+H]^+$
N-Piperidinyl Etonitazene	$C_{23}H_{28}N_4O_3$	408.5	408	409.2234

3. SAMPLE HISTORY

To date, *N*-Piperidinyl Etonitazene was identified in three cases in October 2021. The geographical and demographical breakdown is below:

Geographical Location: New Jersey (n=3)

Biological Sample: Serum (n=3)

Date of First Receipt: October 2021

Other Notable Findings: Fentanyl (n=2), *para*-Fluorofentanyl (n=1)

4. BRIEF DESCRIPTION

N-Piperidinyl Etonitazene is classified as a novel opioid of the benzimidazole sub-class and is structurally dissimilar from fentanyl. Novel opioids have been reported to cause psychoactive effects similar to heroin, fentanyl, and other opioids. Novel opioids have also caused adverse events, including death, as described in the literature. Structurally similar compounds include etonitazene, metonitazene, and isotonitazene. Etonitazene and its analogue synthetic opioids were first synthesized and reported in the literature in the 1950s.[1] Data suggest that this group of analogues can have potency similar to or greater than fentanyl.[2,3] Recent *in vitro* data suggest that *N*-piperidinyl etonitazene is slightly less potent than etonitazene but more potent than fentanyl (unpublished data from M. Vandeputte and C. Stove). *N*-Piperidinyl Etonitazene is not explicitly scheduled in the United States; however, etonitazene and isotonitazene are Schedule I substances.

5. ADDITIONAL RESOURCES

1. Hunger, A; Kebrle, J; Rossi, A; Hoffmann, K. (1957) Synthesis of analgesically active benzimidazole derivatives with basic substitutions. *Experientia*, **13**, 400-401. https://link.springer.com/article/10.1007/BF02161116

2. Hoffmann, K; Hunger, A; Rossi, A. (3 May 1960). "Patent US2935514A – Benzimidazoles." https://patents.google.com/patent/US2935514A/en

3. Vandeputte, MM; Van Uytfanghe, K; Layle, NK; St. Germaine, DM; Iula, DM; Stove , CP. Synthesis, Chemical Characterization, and μ-Opioid Receptor Activity Assessment of the Emerging Group of "Nitazene" 2-Benzylbenzimidazole Synthetic Opioids. *ACS Chem. Neurosci*. 2021. https://pubs.acs.org/doi/10.1021/acschemneuro.1c00064

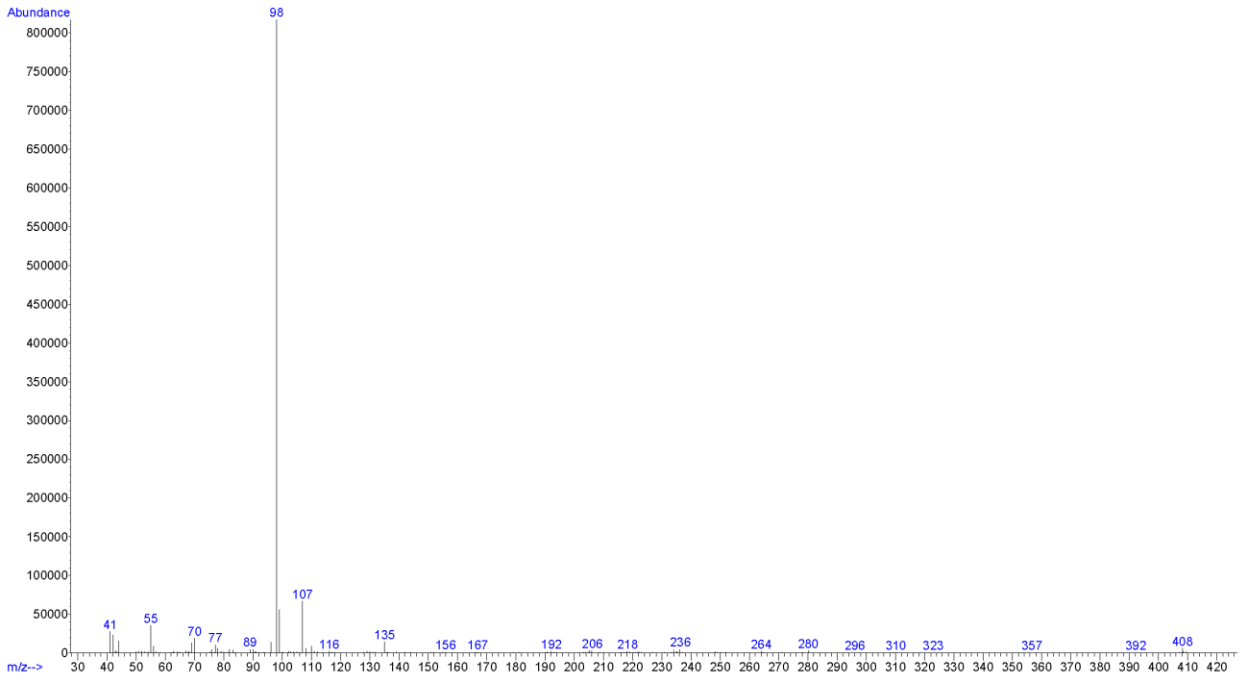
https://www.caymanchem.com/product/33168/n-piperidinyl-etonitazene-(citrate)

6. QUALITATIVE DATA

6.1 GAS CHROMATOGRAPHY MASS SPECTROMETRY (GC-MS)

Testing Performed At:	The Center for Forensic Science Research and Education at the Fredric Rieders Family Foundation (Willow Grove, PA)
Sample Preparation:	Standard diluted in methanol
Instrument:	Agilent 5975 Series GC/MSD System
Standard:	Reference material for *N*-Piperidinyl Etonitazene (Batch: 0610520-5) was purchased from Cayman Chemical Company (Ann Arbor, MI, USA). (https://www.caymanchem.com/product/33168/n-piperidinyl-etonitazene-(citrate))

EI (70 eV) Mass Spectrum: *N*-Piperidinyl Etonitazene (Standard)

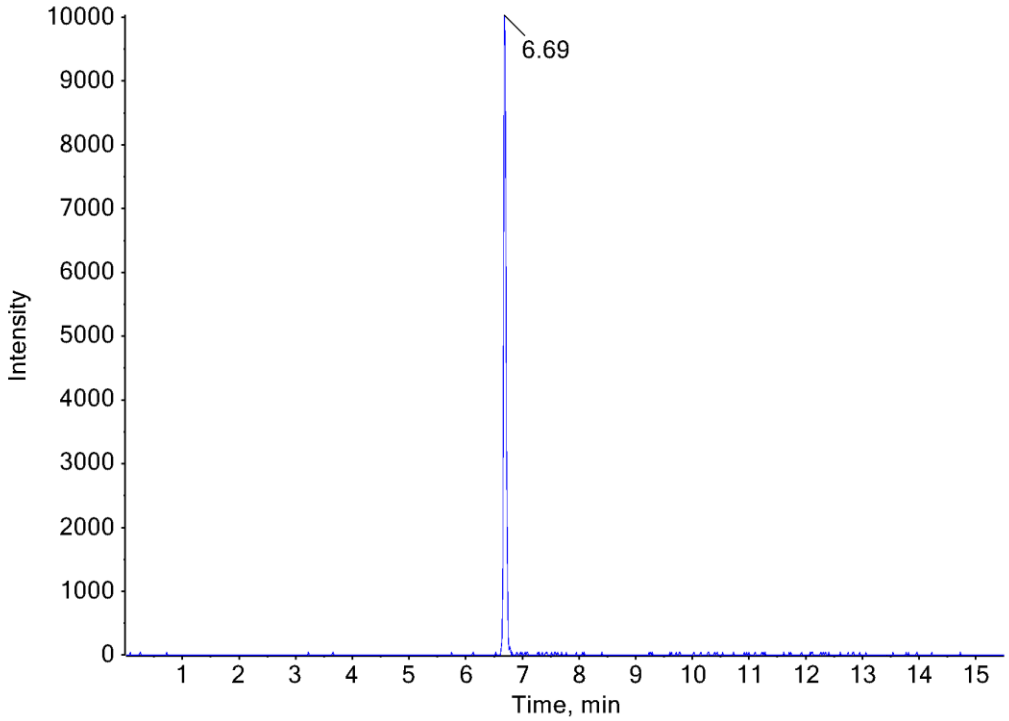


6.2 LIQUID CHROMATOGRAPHY QUADRUPOLE TIME-OF-FLIGHT MASS SPECTROMETRY (LC-QTOF-MS)

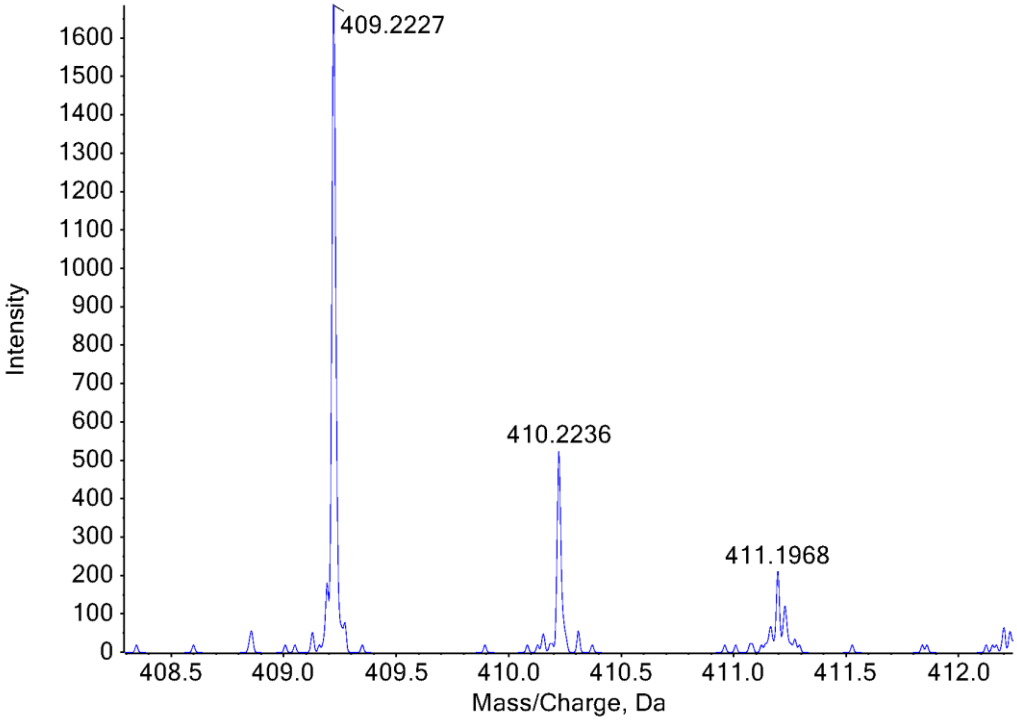
Testing Performed At:	The Center for Forensic Science Research and Education at the Fredric Rieders Family Foundation (Willow Grove, PA)
Sample Preparation:	Liquid-liquid extraction (LLE) – diluted 2+3 with DI H_2O
Instrument:	Sciex TripleTOF® 5600+, Shimadzu Nexera XR UHPLC
Column:	Phenomenex® Kinetex C18 (50 mm x 3.0 mm, 2.6 µm)
Mobile Phase:	A: Ammonium formate (10 mM, pH 3.0)
	B: Methanol/acetonitrile (50:50)
	Flow rate: 0.4 mL/min
Gradient:	Initial: 95A:5B; 5A:95B over 13 min; 95A:5B at 15.5 min
Temperatures:	Autosampler: 15 °C
	Column Oven: 30 °C

	Source Heater: 600 °C
Injection Parameters:	Injection Volume: 10 µL
QTOF Parameters:	TOF MS Scan Range: 100-510 Da
	Precursor Isolation: SWATH® acquisition (27 windows)
	Fragmentation: Collison Energy Spread (35±15 eV)
	MS/MS Scan Range: 50-510 Da
Retention Time:	6.69 min
Standard Comparison:	Reference material for *N*-Piperidinyl Etonitazene (Batch: 0610520-5) was purchased from Cayman Chemical Company (Ann Arbor, MI, USA). Analysis of this standard resulted in positive identification of the analyte in the extract as *N*-Piperidinyl Etonitazene, based on retention time (6.65 min) and mass spectral data. (https://www.caymanchem.com/product/33168/n-piperidinyl-etonitazene-(citrate))

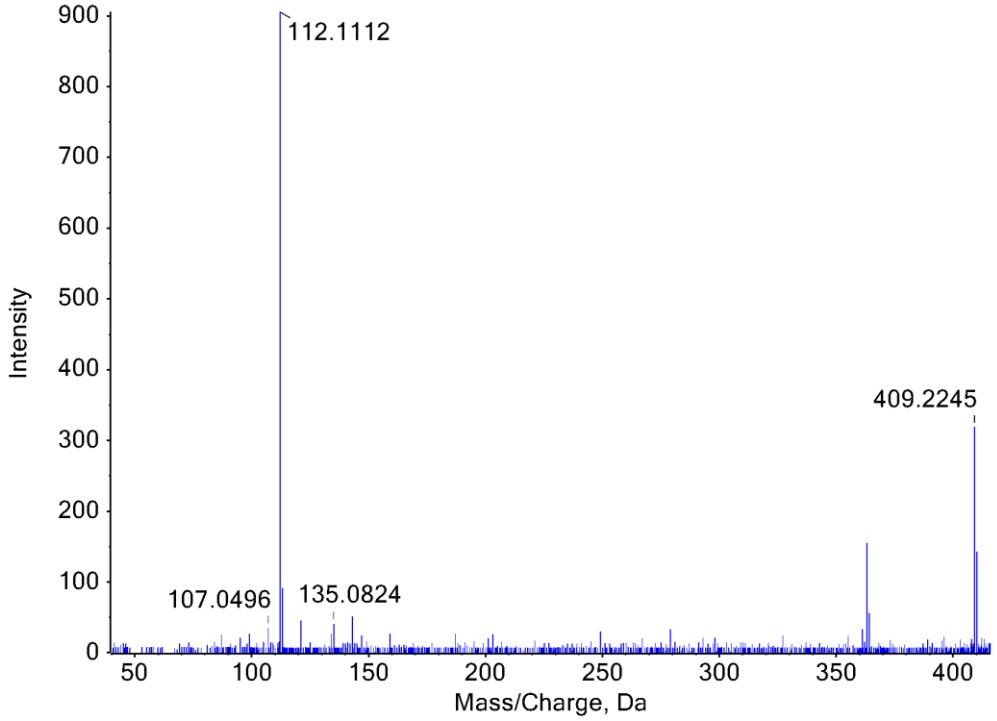
Extracted Ion Chromatogram: *N*-Piperidinyl Etonitazene



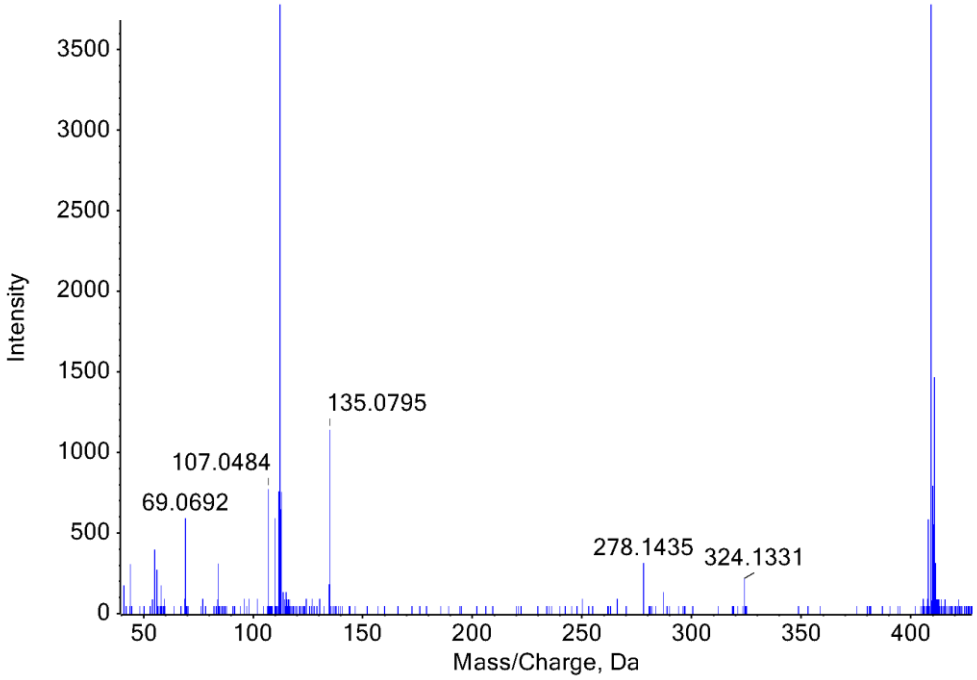
TOF MS Spectra: *N*-Piperidinyl Etonitazene



MS/MS Spectra: *N*-Piperidinyl Etonitazene



MS/MS Spectra: *N*-Piperidinyl Etonitazene (Standard – 10x Zoom)



7. FUNDING

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