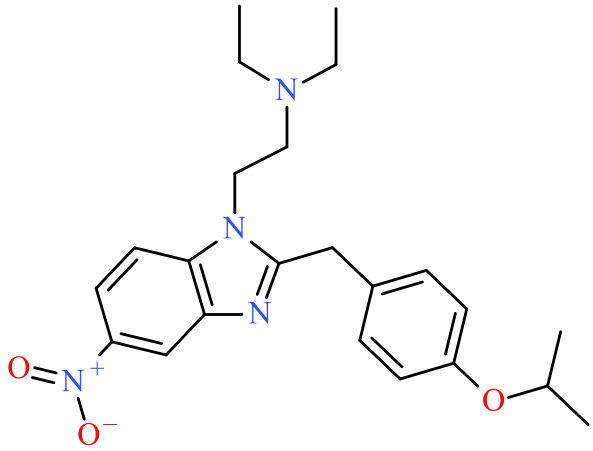
Isotonitazene

Sample Type: **Biological Fluid**



Latest Revision: **November 21, 2019**

Date of Report: **November 19, 2019**

1. GENERAL INFORMATION

IUPAC Name: N,N-diethyl-2-[2-[(4-isopropoxyphenyl)methyl]-5-nitro-benzimidazol-1-yl]ethanamine

InChI String: InChI=1S/C23H30N4O3/c1-5-25(6-2)13-14-26-22-12-9-19(27(28)29)16-21(22)24-23(26)15-18-7-10-20(11-8-18)30-17(3)4/h7-12,16-17H,5-6,13-15H2,1-4H3

CFR: Not Scheduled (11/2019)

CAS# 14188-81-9

Synonyms: None Available

Source: NMS Labs – Toxicology Department

2. CHEMICAL DATA

Analyte	Chemical Formula	Molecular Weight	Molecular Ion [M^+]	Exact Mass $[M+H]^+$
Isotonitazene	$C_{23}H_{30}N_4O_3$	410.5	410	411.2391

***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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3. SAMPLE HISTORY

Isotonitazene has been identified in eight cases since August 2019. The geographical and demographical breakdown is below:

Geographical Location: Illinois (n=4), Indiana (n=4)

Biological Sample: Blood (n=8)

Date of First Receipt: August 20, 2019

Other Notable Findings: Etizolam (n=6), Fentanyl (n=3), U-47700 (n=1), Piperidylthiambutene (n=1)

4. BRIEF DESCRIPTION

Isotonitazene is classified as a novel opioid but is dissimilar from fentanyl and U-series analogues. Novel opioids have been reported to cause psychoactive effects similar to heroin, fentanyl, and other opioids. Novel opioids have also caused adverse events, including deaths, as described in the literature. Structurally similar compounds to isotonitazene include etonitazene, metonitazene, and clonitazene. These synthetic opioids were first synthesized and reported in the literature in the 1950s.[1] Data suggests that this group of analogues have potency similar to or greater than fentanyl.[2] Etonitazene is reported to be the most potent followed by isotonitazene and metonitazene. Isotonitazene is not explicitly a scheduled substance in the United States; however, etonitazene and clonitazene are Schedule I substances. Identifications of isotonitazene have been previously reported in Canada (Alberta) and Europe (Belgium) from both seized drug and toxicology casework.

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.proxyiub.uits.iu.edu/article/10.1007/BF02161116

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

https://www.caymanchem.com/product/27255

6. QUALITATIVE DATA

6.1 GAS CHROMATOGRAPHY MASS SPECTROMETRY (GC-MS)

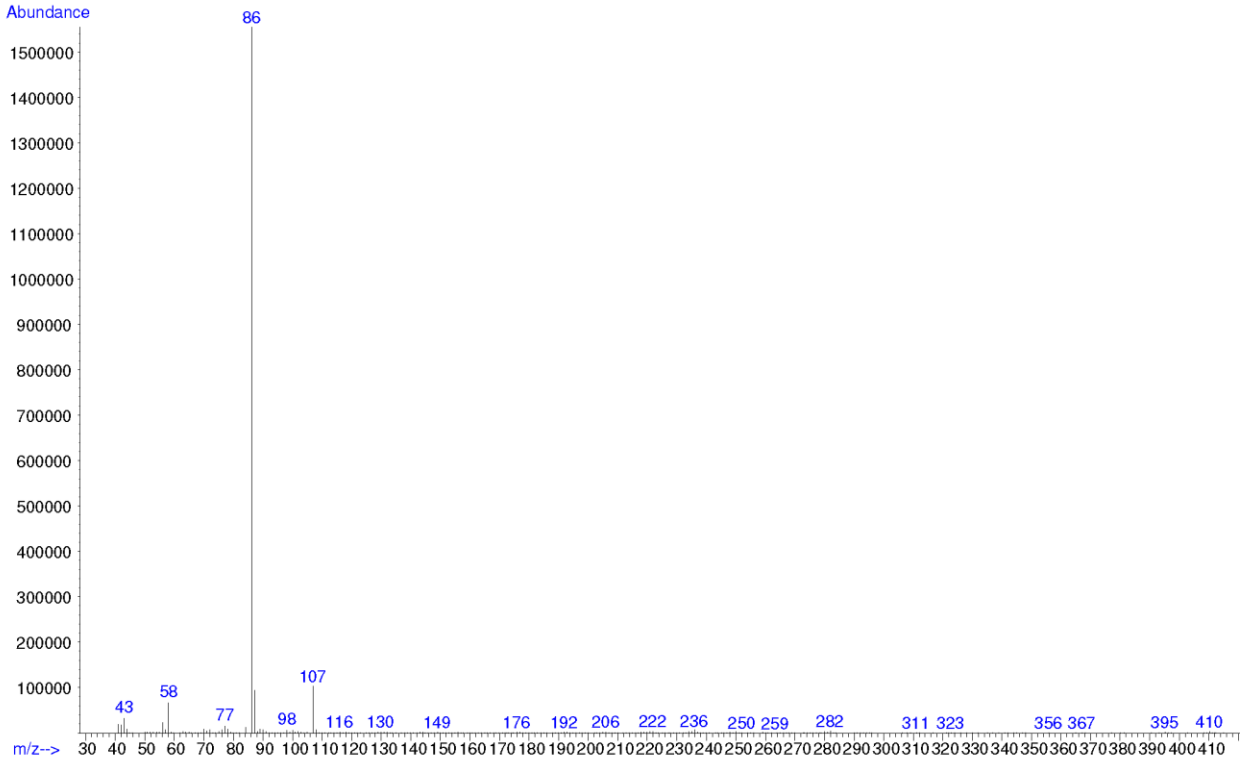
Testing Performed At: The Center for Forensic Science Research and Education at the Fredric Rieders Family Foundation (Willow Grove, PA)

Sample Preparation: Standard diluted in methanol

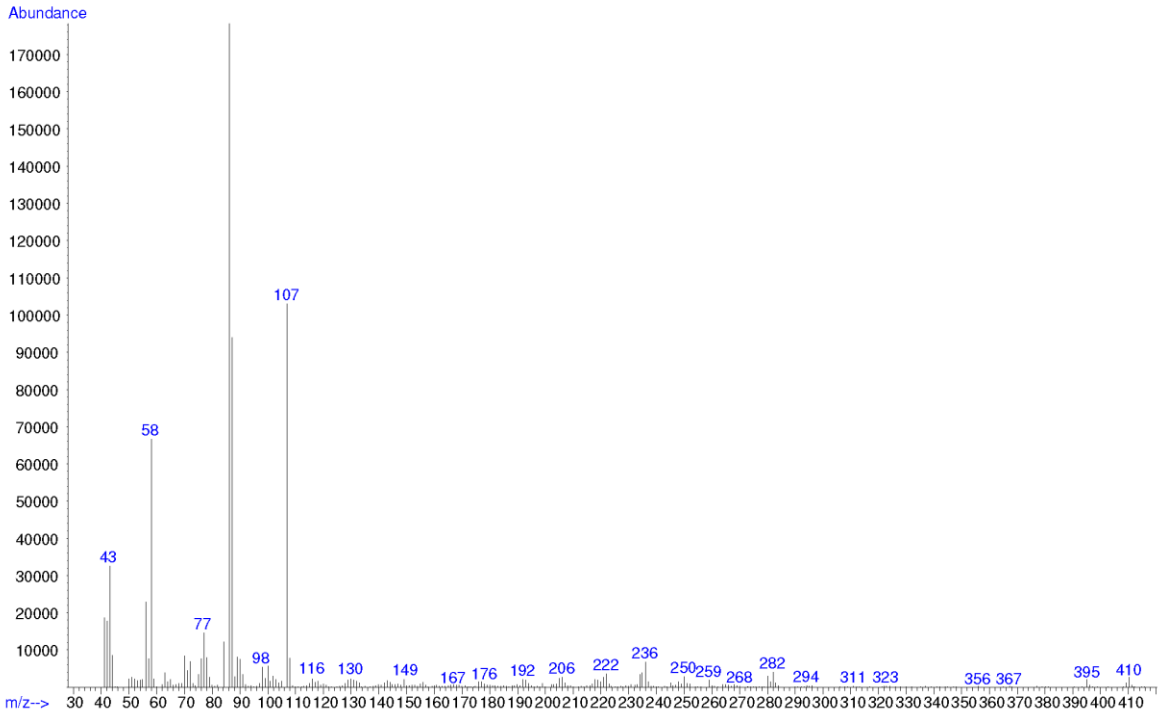
Instrument: Agilent 5975 Series GC/MSD System

Standard: Reference material for Isotonitazene (Batch: 0557801-5) was purchased from Cayman Chemical (Ann Arbor, MI, USA). (https://www.caymanchem.com/product/27255)

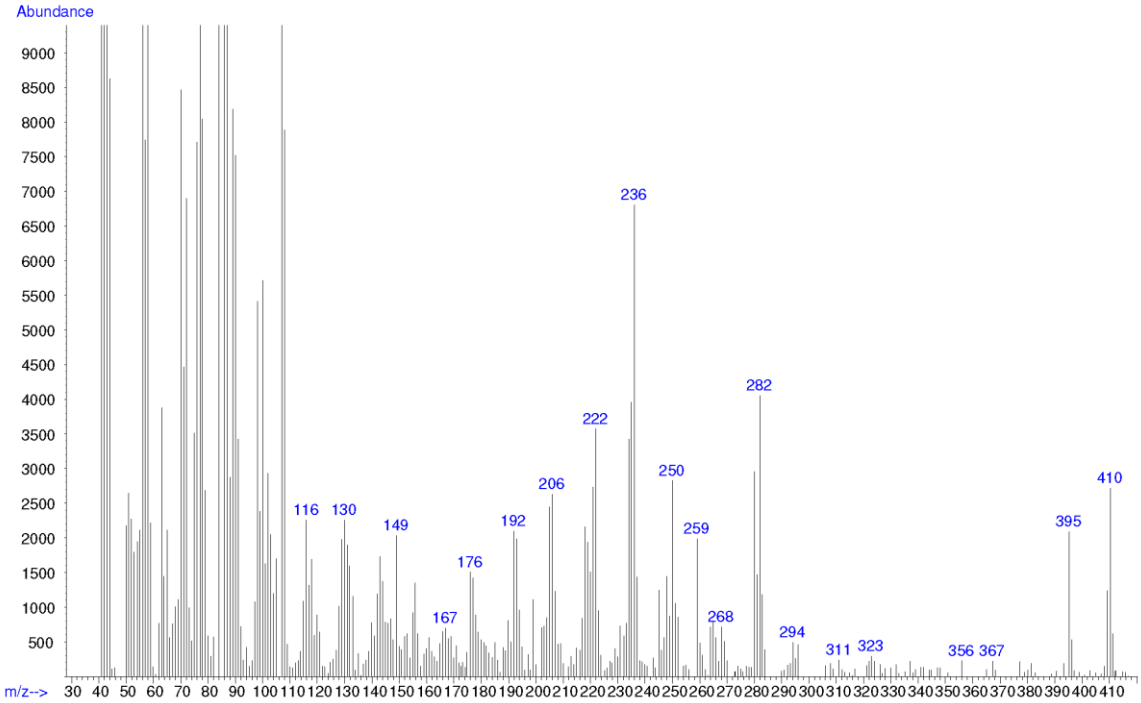
EI (70 eV) Mass Spectrum: Isotonitazene (Standard)



EI (70 eV) Mass Spectrum (10x Zoom): Isotonitazene (Standard)



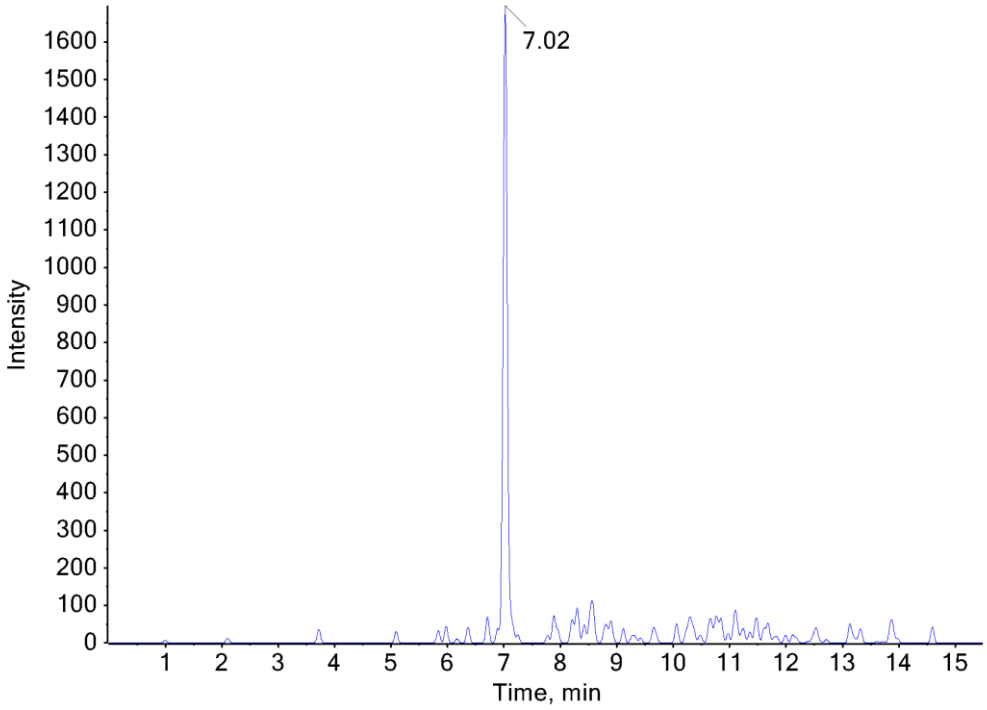
EI (70 eV) Mass Spectrum (100x Zoom): Isotonitazene (Standard)



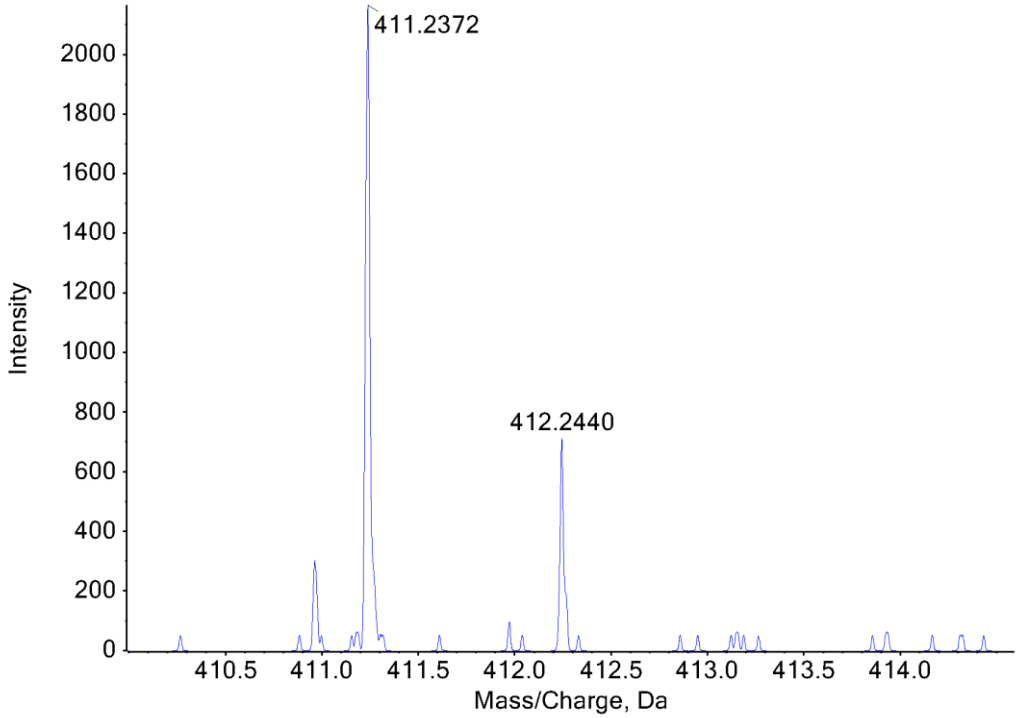
6.2 LIQUID CHROMATOGRAPHY QUADRUPOLE TIME-OF-FLIGHT MASS SPECTROMETRY (LC-QTOF-MS)

Testing Performed At:	The Center for Forensic Science Research and Education at the Fredric Rieders Family Foundation (Willow Grove, PA)
Sample Preparation:	No additional preparation - direct analysis of sample extract
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:	7.02 min
Standard Comparison:	Reference material for Isotonitazene (Batch: 0557801-5) 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 Isotonitazene, based on retention time (6.95 min) and mass spectral data. (https://www.caymanchem.com/product/27255)

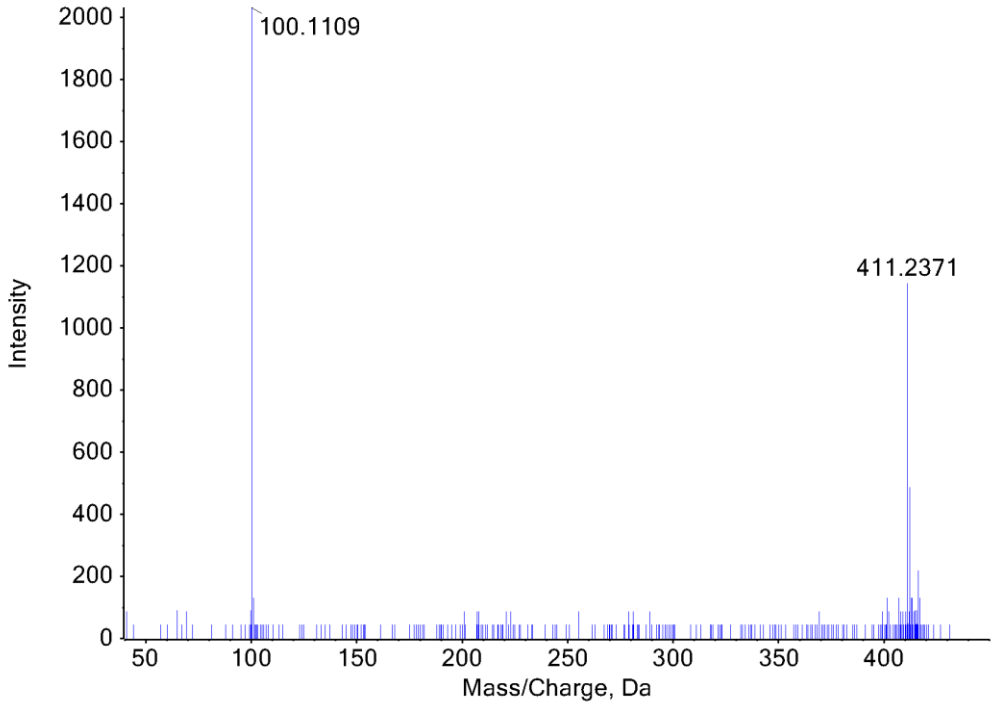
Extracted Ion Chromatogram: Isotonitazene (Biological Sample)



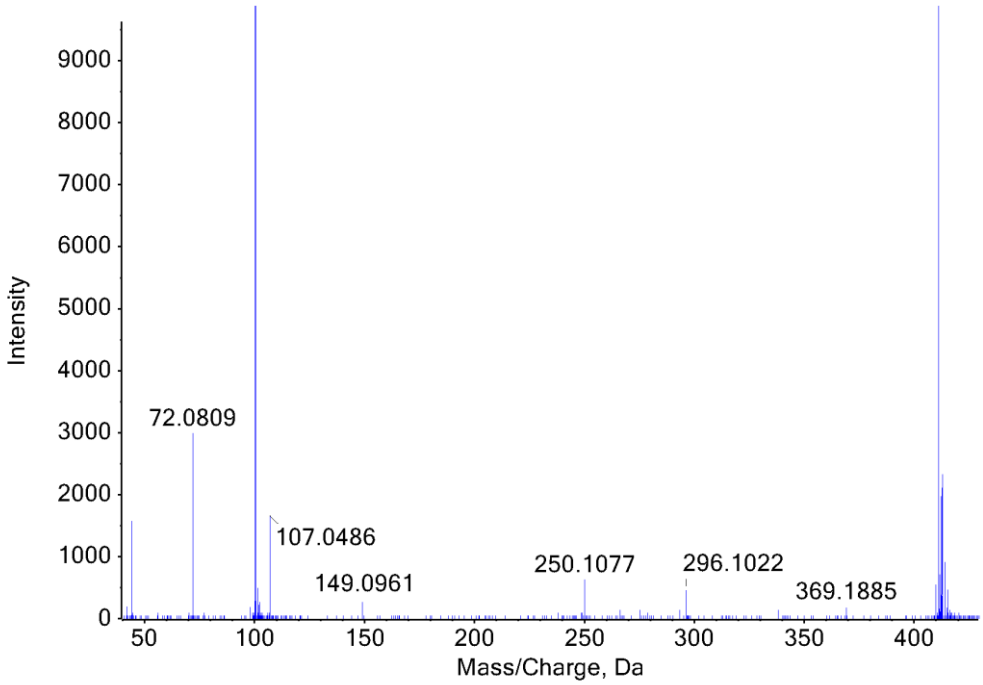
TOF MS Spectrum: Isotonitazene (Biological Sample)



MS/MS Spectrum: Isotonitazene (Biological Sample)



MS/MS Spectrum (10x Zoom): Isotonitazene (Standard)



7. FUNDING

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8. REVISION HISTORY

Date	Revision
11/21/2019	Revised Brief Description: “Isotonitazene is not explicitly a scheduled substance in the United States; however, etonitazene and clonitazene are Schedule I substances.”