

Short Communication for the Analysis of Isotonitazene

Date: May 2020

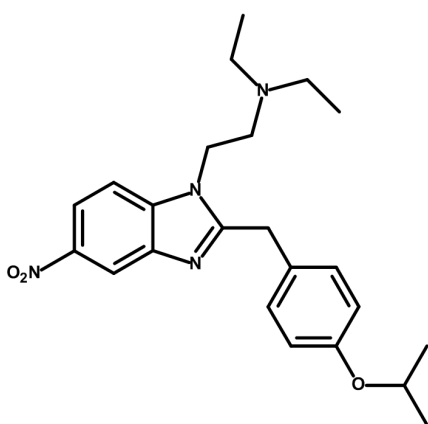
Synonyms:

N,N-diethyl-2-[[4-(1-methylethoxy)phenyl]methyl]-5-nitro-1H-benzimidazole-1-ethanamine

N,N-diethyl-2-[5-nitro-2-(4-[(propan-2-yl)oxy]phenyl)methyl)-1H-benzimidazol-1-yl]ethan-1-amine

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

Structure:



Formula: C₂₃H₃₀N₄O₃

Molecular Weight (nominal mass): 410.23

Theoretical M+H accurate mass: 411.2391

Pharmacological Drug Class: Opioid

Suggested LOD: 0.05 ng/mL

Suggested LOQ: 0.1 ng/mL

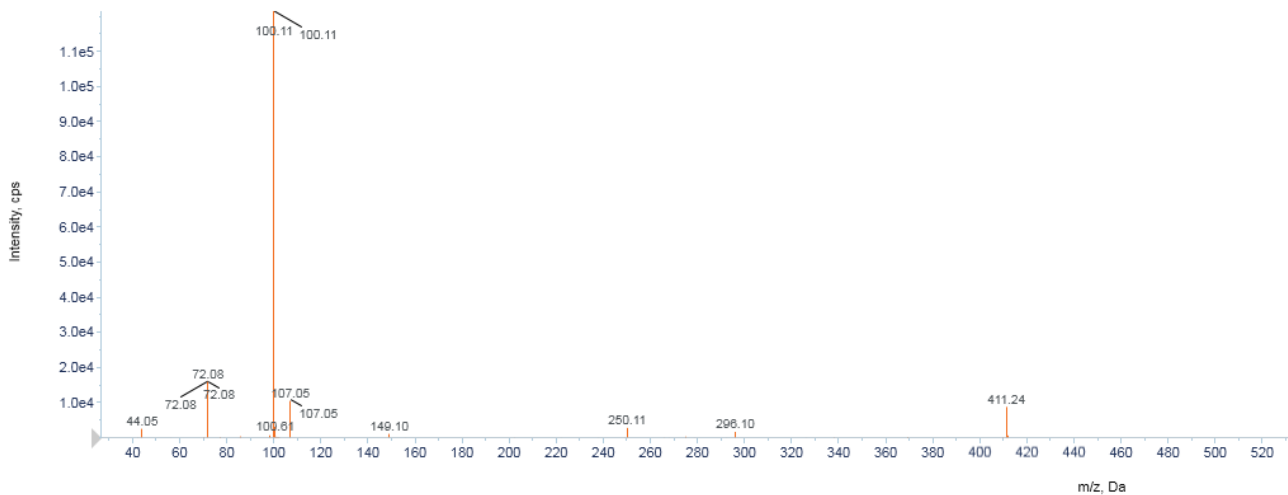
Isotonitazene is a nitrobenzimidazole synthetic opioid chemically related to the internationally controlled substance etonitazene. Isotonitazene has been shown to be a potent mu-opioid receptor agonist. Isotonitazene was first identified since mid-2019 in Europe, the USA and Canada with increasing detections throughout 2019 and into 2020. Case reports indicate it may be encountered as a white powder associated with heroin use, similar to recent other synthetic opioids such as U-opioids and fentanils.

From the United Nations Office on Drugs and Crime (UNODC) ToxPortal, isotonitazene has been reported in 8 fatalities in the USA with post-mortem blood concentrations between 0.4 and 4.4 ng/mL. In 18 recently published cases from the USA, isotonitazene was found at concentrations between 0.4 and 9.5 ng/mL (median 1.75 ng/mL) in post-mortem blood, in urine the range was 0.4-6.0 ng/mL and vitreous humour, 0.1 ng/mL. These were somewhat comparable to measured

concentrations in cases from Canada, in particular blood concentrations of 0.12 and 0.56 ng/mL. All these data indicate expected very low biological fluid concentrations as for other potent synthetic opioids.

Metabolite discovery during case studies have demonstrated that isotonitazene undergoes dealkylation to form N-desalkyl and O-desalkyl metabolites with N-desethyl-isotonitazene and N-desethyl-O-desalkyl-isotonitazene as primary metabolites especially in urine. 5-Amino-isotonitazene was identified as a common metabolite in blood.

LC-QTOF-MS Spectrum:



[source: Orange County Crime Lab, Santa Ana, CA, USA]

References:

Blanckaert P, Cannaert A, Van Uytvanghe K, Hulpia F, Deconinck E, Van Calenbergh S, Stove C. Report on a novel emerging class of highly potent benzimidazole NPS opioids: Chemical and in vitro functional characterization of isotonitazene. *Drug Test Anal.* (2020) 12(4):422-430

EMCDDA initial report on the new psychoactive substance, isotonitazene (April 2020)
https://www.emcdda.europa.eu/system/files/publications/13028/EMCDDA-Initial-report_Isotonitazene.pdf

Krotulski AJ, Papsun DM, Kacinko SL, Logan BK. Isotonitazene Quantitation and Metabolite Discovery in Authentic Forensic Casework. *J Anal Toxicol.* 2020 Feb 24. pii: bkaa016. doi: 10.1093/jat/bkaa016. [Epub ahead of print]