

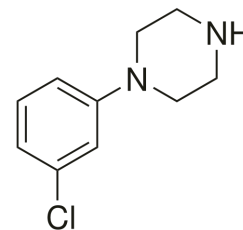
NEW DRUG: meta-Chlorophenylpiperazine (mCPP)

Kevin G. Shanks, kshanks@aitlabs.com AIT Laboratories 2265 Executive Drive, Indianapolis, IN 46241

1-(3-chlorophenyl) piperazine, or mCPP, is a piperazine metabolite of the drugs Trazodone (Desyre[®]), Nefazodone (Serzone[®]), Mepiprazole (Psigodal[®]) and the discontinued drug, Etoperidone [1]. The piperazine class of drugs is a broad class of analytes that share a piperazine functional group (a six-membered ring containing two opposing nitrogen atoms). Many of these drugs act as antidepressants, antihistamines, antipsychotics, urologicals, and other recreational drugs of abuse [1]. mCPP is also a recreational drug that is available in tablet form, which is consumed orally, or powder form, which is snorted or injected [2]. Pharmacologically, mCPP acts as a serotonin receptor agonist, which leads to antidepressant and anxiolytic properties, as well as hallucinogenic side effects [3,4]. Due to its important pharmacological activity and potential abuse, the drug was added to AIT Laboratories' comprehensive panel of drugs in 2008. In routine casework, mCPP has been detected in 266 postmortem cases and whole blood concentrations ranged from 5-1,325 ng/mL. Tissue (liver) specimen concentrations ranged from 1,722-27,831 ng/g. In every case, mCPP was detected with the presence of either Nefazodone (2 cases) or Trazodone (264 cases). Analytical reference standards can be purchased from Cerilliant Corporation (C-089), Sigma-Aldrich, Inc. (125180), and/or Toronto Research Chemicals, Inc. (C379590). A deuterated analog is also available from Toronto Research Chemicals, Inc. (C379592). mCPP is chemically related to other illicit piperazine drugs, such as BZP and TFMPP.

General Information

IUPAC Name: 1-(3-chlorophenyl)piperazine
Common Name: 1-(m-chlorophenyl)piperazine; mCPP; m-CPP; 1-3-CPP
Appearance: Research chemical is a pale orange oil or diluted in methanol
Illicit drug is sold in tablet form in a variety of colors
Chemical Formula: C₁₀H₁₃ClN₂
Molecular Weight: 196.6 g/mol
CAS Number: 6640-24-0



Pharmacology

Half-Life: 2-7 hours
Elimination: Eliminated in the urine as a hydroxylated metabolite and hydroxylated glucuronide conjugate [5]
Mechanism of Action: Acts as an agonist for 5-HT receptors as well as the serotonin transporter protein; also has affinity for the α -adrenergic receptors.

Analytical Toxicology

LC-ToF Screening Analysis: Following a protein precipitation extraction with acetonitrile; Limit of detection (LOD) is 1 ng/mL
Theoretical accurate [M+H]⁺ is 197.0846 (Figure 1)
LC/MS/MS Confirmatory Analysis: Following a protein precipitation with acetonitrile
Linearity 5 ng/mL – 2,000 ng/mL; Quadratic curve fit;
mCPP d8 as an internal standard
Quantitative MRM is 197.16 \Rightarrow 118.20
Qualitative MRM is 197.16 \Rightarrow 43.91 (Figure 2)

Also can be detected by both GC/NPD & GC/MS with a routine basic drug screen:
Chlorobutane basic drug extraction with acidic back extraction
Detection on both the GC/NPD and GC/MS

NEW DRUG: meta-Chlorophenylpiperazine (mCPP)

GC/MS ions 154, 196, 156, 138 (Figure 3)

Relative retention time Bupropion, **mCPP**, Meperidine, Diphenhydramine

Quantitative method validation not performed

References

1. Baselt, R.C., The disposition of toxic drugs and chemicals in man. 8th ed. 2008, Foster City: Biomedical Publications.
2. Kovaleva, Julia, et. al., Acute chlorophenylpiperazine overdose: a case report and review of the literature. *Ther. Drug Monit.* 2008;20:394-398. PMID 18520613.
3. Silverstone, PH et. al., The effects of administration of mCPP on psychological, cognitive, cardiovascular, hormonal and MHPG measurements in human volunteers. *Int Clin Psychopharmacol.* 1994 Sep;9(3): 173-178. PMID 7814826.
4. Kahn, RS, Wetzler S. m-Chlorophenylpiperazine as a probe of serotonin function. *Biol Psychiatry.* 1991 Dec 1;30(11): 1139-1166. PMID 1663792.
5. Rotzinger S, et. al., Human CYP2D6 and metabolism of m-chlorophenylpiperazine. *Biol Psychiatry.* 1998 Dec 1;44(11): 1185-1191. PMID 9836023.

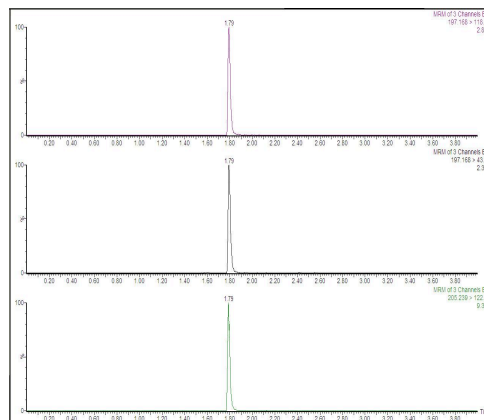
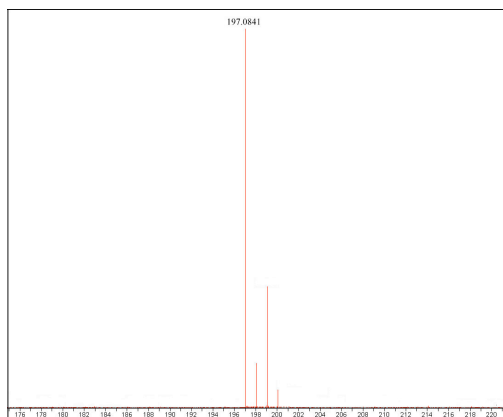


Figure 1 - LC-ToF Extracted Ion Spectrum (XIS) of mCPP in Postmortem Whole Blood

Figure 2 - Confirmatory Analysis of mCPP by LC/MS/MS – Postmortem Whole Blood Specimen (26.8 ng/mL)

NEW DRUG: meta-Chlorophenylpiperazine (mCPP)

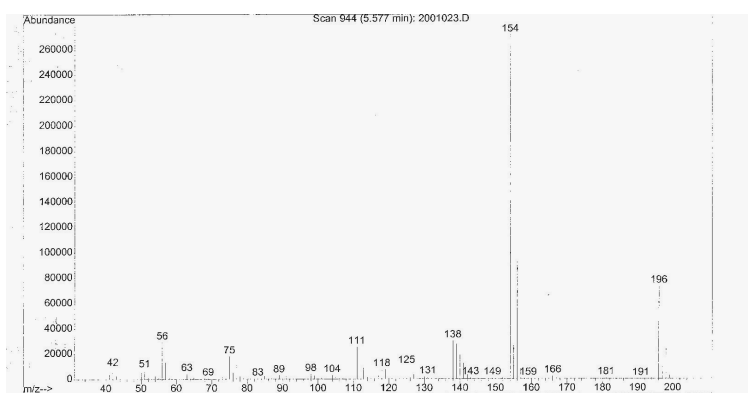


Figure 3 – EI Mass Spectra of mCPP