Mass Spectra of Select Benzyl- and Phenyl- Piperazine Designer Drugs

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ABSTRACT: The mass spectra of five piperazine designer drugs (N-benzylpiperazine, 1-(3,4-methylenedioxy-benzyl)piperazine, 1-(3-trifluoromethylphenyl)piperazine, 1-(3-chlorophenyl)piperazine, and 1-(4-methoxy-phenyl)piperazine) and their trimethylsilyl derivatives are presented.

KEYWORDS: Benzylpiperazines, Phenylpiperazines, Designer Drugs, Mass Spectrometry, Trimethylsilylation, Forensic Chemistry

Designer drugs of the benzyl- or phenyl- piperazine type, i.e., benzylpiperazine (BZP) itself, its methylenedioxy analogue 1-(3,4-methylenedioxybenzyl)piperazine (MDBP), 1-(3-trifluoromethylphenyl)piperazine (TFMPP), 1-(3-chlorophenyl)piperazine (mCPP), and 1-(4-methoxyphenyl)piperazine (MeOPP), recently have gained popularity and notoriety. Seizures have been made throughout the world (1-9), and a few fatalities have been reported (10-11). The increasing abuse of piperazines in the United States resulted in the temporary placement of BZP and TFMPP into Schedule I of the Controlled Substances Act (12). BZP was permanently scheduled in March, 2004 (13); however, TFMPP is currently not controlled in the United States.

Recently, many GC/MS studies on the metabolites of piperazines (i.e., from biological fluids) and/or their acetyl or heptafluorobutyryl derivatives have been published (14-24). However, most forensic drug laboratories perform GC/MS on the underivatized or trimethylsilylated derivatives of amine drugs. In Figures 1 and 2, the structures, electron-ionization mass spectra, and gas chromatographic retention indices (recorded on an Agilent GC-MSD 5972, HP-1 column, 12 m x 0.2 mm I.D., 100-310° C, 30° C/minute (25)) of the target piperazines and their trimethylsilyl derivatives are displayed. Additional data for these and several related piperazines will be published elsewhere (26-27).

References

- 1. Roesner P, Junge T, Fritschi G, Klein B, Thielert K, Kozlowski M. Neue synthetische drogen: Piperazin-, procyclidin- und alpha-aminopropiophenon derivate. Toxichem. Krimtech. 1999;66:81-90.
- 2. de Boer D, Bosman IJ, Hidvegi E, Manzoni C, Benko AA, Dos RL, Maes RA. Piperazine-like compounds: A new group of designer drugs-of-abuse on the European market. Forensic Sci. Int. 2001;121:47-56.
- 3. U.S. Drug Enforcement Administration Office of Forensic Sciences. Benzylpiperazine (BZP) and N-(3-trifluoromethylphenyl)piperazine (TFMPP). Microgram 2001;34:23.*
- 4. U.S. Drug Enforcement Administration Office of Forensic Sciences. BZP and Nexus tablets. Microgram 2001;34:3.*

- U.S. Drug Enforcement Administration Office of Forensic Sciences. Piperazines in Roanoke, Virginia. Microgram 2001;34:43.*
- 6. U.S. Drug Enforcement Administration Office of Forensic Sciences. Benzylpiperazine and Peyote. Microgram 2001;34:65.*
- 7. U.S. Drug Enforcement Administration Office of Forensic Sciences. Seven unusual tablet submissions in Largo, Florida. Microgram 2001;34:157.*
- 8. U.S. Drug Enforcement Administration Office of Forensic Sciences. 1-Benzylpiperazine (BZP) and N-(3-trifluoromethylphenyl)piperazine (TFMPP). Microgram 2001;34:225.*
- 9. U.S. Drug Enforcement Administration Office of Forensic Sciences. Benzylpiperazine (BZP) and N-(3-trifluoromethylphenyl)piperazine (TFMPP). Microgram 2001;34:196.*
- 10. Balmelli C, Kupferschmidt H, Rentsch K, Schneemann M. [Fatal brain edema after ingestion of ecstasy and benzylpiperazine]. Dtsch. Med. Wochenschr. 2001;126:809-811.
- 11. Wikstrom M, Holmgren P, Ahlner J. A2 (N-benzylpiperazine), a new drug of abuse in Sweden. J. Anal. Toxicol. 2004;28:67-70.
- 12. U.S. Drug Enforcement Administration Department of Justice. Schedules of controlled substances: Temporary placement of benzylpiperazine and trifluoromethylphenylpiperazine into Schedule I. Fed. Register 2002;67:59161-59162.
- 13. U.S. Drug Enforcement Administration Department of Justice. Schedules of controlled substances. Placement of 2,5-dimethoxy-4-(n)-propylthiophenethylamine and N-benzylpiperazine into Schedule I of the Controlled Substances Act. Fed. Register 2004;69:12794-12797.
- 14. Maurer HH, Kraemer T, Springer D, Staack RF. Chemistry, pharmacology, toxicology, and hepatic metabolism of designer drugs of the amphetamine (Ecstasy), piperazine, and pyrrolidinophenone types; a Synopsis. Ther. Drug Monit. 2004;26:127-131.
- 15. Staack RF, Maurer HH. New designer drug 1-(3,4-methylenedioxybenzyl) piperazine (MDBP): Studies on its metabolism and toxicological detection in rat urine using gas chromatography/mass spectrometry. J. Mass Spectrom. 2004;39:255-261.
- Staack RF, Paul LD, Springer D, Kraemer T, Maurer HH. Cytochrome P450 dependent metabolism of the new designer drug 1-(3-trifluoromethylphenyl)piperazine (TFMPP). In vivo studies in Wistar and Dark Agouti rats as well as in vitro studies in human liver microsomes. Biochem. Pharmacol. 2004;67:235-244.
- 17. Staack RF, Theobald DS, Paul LD, Springer D, Kraemer T, Maurer HH. In vivo metabolism of the new designer drug 1-(4-methoxyphenyl)piperazine (MeOPP) in rat and identification of the human cytochrome P450 enzymes responsible for the major metabolic step. Xenobiotica 2004;34:179-192.
- Staack RF, Fritschi G, Maurer HH. New designer drug 1-(3-trifluoromethylphenyl)piperazine (TFMPP): Gas chromatography/mass spectrometry and liquid chromatography/mass spectrometry studies on its phase I and II metabolism, and on its toxicological detection in rat urine. J. Mass Spectrom. 2003;38:971-981.
- 19. Staack RF, Maurer HH. Piperazine-derived designer drug 1-(3-chlorophenyl)piperazine (mCPP): GC-MS studies on its metabolism and its toxicological detection in urine, including analytical differentiation from its precursor drugs trazodone and nefazodone. J. Anal. Toxicol. 2003;27:560-568.

- Staack RF, Fritschi G, Maurer HH. Studies on the metabolism and the toxicological analysis of the new piperazine-like designer drug N-benzylpiperazine in urine using gas chromatography-mass spectrometry. J. Chromatogr. B Analyt. Technol. Biomed. Life Sci. 2002;773:35-46..
- 21. Staack RF, Maurer HH. Studies on the metabolism and the toxicological analysis of the nootropic drug fipexide in rat urine using gas chromatography-mass spectrometry. J. Chromatogr. B Analyt. Technol. Biomed. Life Sci. 2004;804:337-343.
- 22. Staack RF, Theobald DS, Maurer HH. Studies on the human metabolism and the toxicologic detection of the cough suppressant Dropropizine in urine using gas chromatography-mass spectrometry. Ther. Drug Monit. (In Press (2004)).
- 23. Peters FT, Schaefer S, Staack RF, Kraemer T, Maurer HH. Screening for and validated quantification of amphetamines and of amphetamine- and piperazine-derived designer drugs in human blood plasma by gas chromatography/mass spectrometry. J. Mass Spectrom. 2003;38:659-676.
- Staack RF, Maurer HH. Toxicological detection of the new designer drug 1-(4methoxyphenyl)piperazine and its metabolites in urine and differentiation from an intake of structurally related medicaments using gas chromatography-mass spectrometry. J. Chromatogr. B - Analyt. Technol. Biomed. Life Sci. 2003;798:333-342.
- 25. Maurer HH. Methods for GC-MS. (In) Mass Spectral and GC Data of Drugs, Poisons, Pesticides, Pollutants and Their Metabolites, Part 4, Pfleger K, Maurer HH, Weber A, Eds., Wiley-VCH, Weinheim: 2000, pp. 3-241.
- 26. Pfleger K, Maurer HH, Weber A. (In) Mass Spectral and GC Data of Drugs, Poisons, Pesticides, Pollutants and their Metabolites, Part 5, 2nd Ed. Wiley-VCH, Weinheim, 2004, In Preparation.
- 27. Pfleger K, Maurer HH, Weber A. (In) Mass Spectral Library of Drugs, Poisons, Pesticides, Pollutants and their Metabolites, 4th Ed. Agilent Technologies, Palo Alto (CA), 2004, In Preparation.

[Editor's Notes: * All issues of *Microgram* prior to January 2003 are law enforcement restricted. Selected references on the analysis of various piperazines were presented in *Microgram Bulletin* 2004;37(4):76.]

Figure 1: Structures, electron-ionization mass spectra, and gas chromatographic retention indices of underivatized piperazine-derived designer drugs.

Figure 2: Structures, electron-ionization mass spectra, and gas chromatographic retention indices of trimethylsilylated piperazine-derived designer drugs.

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