



INDIANA UNIVERSITY

BORKENSTEIN
COURSE

Center for Studies
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Benzodiazepines and Mass Spectrometry

by
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- Xue, Y.J., J. Pursley, and M.E. Arnold, **A simple 96-well liquid-liquid extraction with a mixture of acetonitrile and methyl t-butyl ether for the determination of a drug in human plasma by high-performance liquid chromatography with tandem mass spectrometry.** J Pharm Biomed Anal, 2004. 34(2): p. 369-78.
- Xu, J. and X. Huang, **Mass spectral fragmentation of 2a,4-disubstituted 2,2a,3,4-tetrahydro-2-phenoxo-1H-azeto[2,1-d][1,5]benzothiazepin-1-ones under electron impact ionization conditions.** Rapid Commun Mass Spectrom, 2004. 18(8): p. 859-62.
- Wallis, M., W.M. Mullett, and J. Pawliszyn, **Monitoring of drugs and metabolites in whole blood by restricted-access solid-phase microextraction coupled to liquid chromatography-mass spectrometry.** J Chromatogr A, 2004. 1025(1): p. 85-92.
- Vanhoenacker, G., et al., **Analysis of benzodiazepines in dynamically coated capillaries by CE-DAD, CE-MS and CE-MS2.** J Pharm Biomed Anal, 2004. 34(3): p. 595-606.
- Smink, B.E., et al., **Quantitative analysis of 33 benzodiazepines, metabolites and benzodiazepine-like substances in whole blood by liquid chromatography-(tandem) mass spectrometry.** J Chromatogr B Analyt Technol Biomed Life Sci, 2004. 811(1): p. 13-20.
- Proenca, P., et al., **Forensic intoxication with clobazam: HPLC/DAD/MSD analysis.** Forensic Sci Int, 2004. 143(2-3): p. 205-9.
- Maurer, H.H., **Advances in analytical toxicology: the current role of liquid chromatography-mass spectrometry in drug quantification in blood and oral fluid.** Anal Bioanal Chem, 2004.
- Laurito, T.L., et al., **Bromazepam determination in human plasma by high-performance liquid chromatography coupled to tandem mass spectrometry: a highly sensitive and specific tool for bioequivalence studies.** J Mass Spectrom, 2004. 39(2): p. 168-76.
- Kratzsch, C., et al., **Screening, library-assisted identification and validated quantification of 23 benzodiazepines, flumazenil, zaleplone, zolpidem and zopiclone in plasma by liquid chromatography/mass spectrometry with atmospheric pressure chemical ionization.** J Mass Spectrom, 2004. 39(8): p. 856-72.
- Kintz, P., M. Villain, and B. Ludes, **Testing for the undetectable in drug-facilitated sexual assault using hair analyzed by tandem mass spectrometry as evidence.** Ther Drug Monit, 2004. 26(2): p. 211-4.
- Kanazawa, H., et al., **Determination of midazolam and its metabolite as a probe for cytochrome P450 3A4 phenotype by liquid chromatography-mass spectrometry.** J Chromatogr A, 2004. 1031(1-2): p. 213-8.
- Hori, Y., et al., [Practical analysis of toxic substances useful for clinical toxicology--10--benzodiazepine]. Chudoku Kenkyu, 2004. 17(2): p. 163-8.
- Gunnar, T., et al., **Validated semiquantitative/quantitative screening of 51 drugs in whole blood as silylated derivatives by gas chromatography-selected ion monitoring mass spectrometry and gas chromatography electron capture detection.** J Chromatogr B Analyt Technol Biomed Life Sci, 2004. 806(2): p. 205-19.
- Bugey, A. and C. Staub, **Rapid analysis of benzodiazepines in whole blood by high-performance liquid chromatography: use of a monolithic column.** J Pharm Biomed Anal, 2004. 35(3): p. 555-62.

- Zeng, H., Y. Deng, and J.T. Wu, **Fast analysis using monolithic columns coupled with high-flow on-line extraction and electrospray mass spectrometric detection for the direct and simultaneous quantitation of multiple components in plasma.** J Chromatogr B Analyt Technol Biomed Life Sci, 2003. 788(2): p. 331-7.
- Wood, M., et al., **Development of a rapid and sensitive method for the quantitation of benzodiazepines in Calliphora vicina larvae and puparia by LC-MS-MS.** J Anal Toxicol, 2003. 27(7): p. 505-12.
- Wang, J., et al., **Simple and sensitive liquid chromatography/tandem mass spectrometry method for the determination of diazepam and its major metabolites in rat cerebrospinal fluid.** Rapid Commun Mass Spectrom, 2003. 17(6): p. 519-25.
- Ugland, H.G., M. Krogh, and L. Reubsæet, **Three-phase liquid-phase microextraction of weakly basic drugs from whole blood.** J Chromatogr B Analyt Technol Biomed Life Sci, 2003. 798(1): p. 127-35.
- Toyo'oka, T., et al., **Determination of hypnotic benzodiazepines (alprazolam, estazolam, and midazolam) and their metabolites in rat hair and plasma by reversed-phase liquid-chromatography with electrospray ionization mass spectrometry.** J Pharm Biomed Anal, 2003. 30(6): p. 1773-87.
- Terada, M., et al., **Simultaneous determination of flunitrazepam and 7-aminoflunitrazepam in human serum by ion trap gas chromatography-tandem mass spectrometry.** Leg Med (Tokyo), 2003. 5 Suppl 1: p. S96-S100.
- Shiran, M.R., et al., **Determination of midazolam and 1'-hydroxymidazolam by liquid chromatography-mass spectrometry in plasma of patients undergoing methadone maintenance treatment.** J Chromatogr B Analyt Technol Biomed Life Sci, 2003. 783(1): p. 303-7.
- Scott, K.S. and Y. Nakahara, **A study into the rate of incorporation of eight benzodiazepines into rat hair.** Forensic Sci Int, 2003. 133(1-2): p. 47-56.
- Schellen, A., et al., **Generic solid phase extraction-liquid chromatography-tandem mass spectrometry method for fast determination of drugs in biological fluids.** J Chromatogr B Analyt Technol Biomed Life Sci, 2003. 788(2): p. 251-9.
- Rivera, H.M., et al., **Application of liquid chromatography-tandem mass spectrometry to the analysis of benzodiazepines in blood.** Eur J Mass Spectrom (Chichester, Eng), 2003. 9(6): p. 599-607.
- Pihlainen, K., E. Sippola, and R. Kostianen, **Rapid identification and quantitation of compounds with forensic interest using fast liquid chromatography-ion trap mass spectrometry and library searching.** J Chromatogr A, 2003. 994(1-2): p. 93-102.
- Negrusz, A. and R.E. Gaensslen, **Analytical developments in toxicological investigation of drug-facilitated sexual assault.** Anal Bioanal Chem, 2003. 376(8): p. 1192-7.
- Negrusz, A., et al., **Elimination of 7-aminoclonazepam in urine after a single dose of clonazepam.** Anal Bioanal Chem, 2003. 376(8): p. 1198-204.
- Moriya, F. and Y. Hashimoto, **Tissue distribution of nitrazepam and 7-aminonitrazepam in a case of nitrazepam intoxication.** Forensic Sci Int, 2003. 131(2-3): p. 108-12.
- Marquet, P., et al., **Comparison of a preliminary procedure for the general unknown screening of drugs and toxic compounds using a quadrupole-linear ion-trap mass spectrometer with a liquid chromatography-mass spectrometry reference technique.** J Chromatogr B Analyt Technol Biomed Life Sci, 2003. 789(1): p. 9-18.

- Kroener, L., F. Musshoff, and B. Madea, **Evaluation of immunochemical drug screenings of whole blood samples. A retrospective optimization of cutoff levels after confirmation-analysis on GC-MS and HPLC-DAD.** *J Anal Toxicol*, 2003. 27(4): p. 205-12.
- Kapron, J.T., et al., **Quantitation of midazolam in human plasma by automated chip-based infusion nanoelectrospray tandem mass spectrometry.** *Rapid Commun Mass Spectrom*, 2003. 17(18): p. 2019-26.
- Jourdil, N., et al., **Automated solid-phase extraction and liquid chromatography-electrospray ionization-mass spectrometry for the determination of flunitrazepam and its metabolites in human urine and plasma samples.** *J Chromatogr B Analyt Technol Biomed Life Sci*, 2003. 788(2): p. 207-19.
- Hager, J.W. and J.C. Yves Le Blanc, **Product ion scanning using a Q-q-Q linear ion trap (Q TRAP) mass spectrometer.** *Rapid Commun Mass Spectrom*, 2003. 17(10): p. 1056-64.
- Gergov, M., I. Ojanpera, and E. Vuori, **Simultaneous screening for 238 drugs in blood by liquid chromatography-ion spray tandem mass spectrometry with multiple-reaction monitoring.** *J Chromatogr B Analyt Technol Biomed Life Sci*, 2003. 795(1): p. 41-53.
- Borrey, D., et al., **Longitudinal study on the prevalence of benzodiazepine (mis)use in a prison: importance of the analytical strategy.** *Addiction*, 2003. 98(10): p. 1427-32.
- Bennett, G.A., E. Davies, and P. Thomas, **Is oral fluid analysis as accurate as urinalysis in detecting drug use in a treatment setting?** *Drug Alcohol Depend*, 2003. 72(3): p. 265-9.
- Wang, P.H., et al., **Improved screen and confirmation test of 7-aminoflunitrazepam in urine specimens for monitoring flunitrazepam (Rohypnol) exposure.** *J Anal Toxicol*, 2002. 26(7): p. 411-8.
- van Hout, M.W., et al., **Feasibility of the direct coupling of solid-phase extraction-pipette tips with a programmed-temperature vaporiser for gas chromatographic analysis of drugs in plasma.** *J Chromatogr B Analyt Technol Biomed Life Sci*, 2002. 766(1): p. 37-45.
- Shou, W.Z., et al., **Ultrafast liquid chromatography/tandem mass spectrometry bioanalysis of polar analytes using packed silica columns.** *Rapid Commun Mass Spectrom*, 2002. 16(17): p. 1613-21.
- Shen, B.H., M. Shen, and X.Y. Zhuo, **[Screening of benzodiazepines and their metabolites in urine].** *Fa Yi Xue Za Zhi*, 2002. 18(1): p. 22-5.
- Samyn, N., et al., **Detection of flunitrazepam and 7-aminoflunitrazepam in oral fluid after controlled administration of rohypnol.** *J Anal Toxicol*, 2002. 26(4): p. 211-5.
- Pirnay, S., et al., **Sensitive method for the detection of 22 benzodiazepines by gas chromatography-ion trap tandem mass spectrometry.** *J Chromatogr A*, 2002. 954(1-2): p. 235-45.
- Negrusz, A., et al., **Deposition of 7-aminoclonazepam and clonazepam in hair following a single dose of Klonopin.** *J Anal Toxicol*, 2002. 26(7): p. 471-8.
- Miki, A., et al., **Simultaneous determination of eleven benzodiazepine hypnotics and eleven relevant metabolites in urine by column-switching liquid chromatography-mass spectrometry.** *J Anal Toxicol*, 2002. 26(2): p. 87-93.
- Maurer, H.H., et al., **Negative ion chemical ionization gas chromatography-mass spectrometry and atmospheric pressure chemical ionization liquid chromatography-mass spectrometry of low-dosed and/or polar drugs in plasma.** *Ther Drug Monit*, 2002. 24(1): p. 117-24.

- Maurer, H.H., **Role of gas chromatography-mass spectrometry with negative ion chemical ionization in clinical and forensic toxicology, doping control, and biomonitoring.** Ther Drug Monit, 2002. 24(2): p. 247-54.
- Levine, B., et al., **Distribution of triazolam and alpha-hydroxytriazolam in a fatal intoxication case.** J Anal Toxicol, 2002. 26(1): p. 52-4.
- Kronstrand, R., et al., **Segmental ion spray LC-MS-MS analysis of benzodiazepines in hair of psychiatric patients.** J Anal Toxicol, 2002. 26(7): p. 479-84.
- Kollroser, M. and C. Schober, **Simultaneous analysis of flunitrazepam and its major metabolites in human plasma by high performance liquid chromatography tandem mass spectrometry.** J Pharm Biomed Anal, 2002. 28(6): p. 1173-82.
- Kintz, P., **A new series of 13 buprenorphine-related deaths.** Clin Biochem, 2002. 35(7): p. 513-6.
- Kemp, P., et al., **Validation of a microtiter plate ELISA for screening of postmortem blood for opiates and benzodiazepines.** J Anal Toxicol, 2002. 26(7): p. 504-12.
- Gu, J.K., et al., **[Identification of estazolam, alprazolam and triazolam in human urine by LC/MSn].** Yao Xue Xue Bao, 2002. 37(2): p. 138-40.
- Deng, Y., et al., **High-speed gradient parallel liquid chromatography/tandem mass spectrometry with fully automated sample preparation for bioanalysis: 30 seconds per sample from plasma.** Rapid Commun Mass Spectrom, 2002. 16(11): p. 1116-23.
- Celinski, R., et al., **[Analytical problems in examination of small amounts of blood samples taken from law offenders].** Arch Med Sadowej Kryminol, 2002. 52(3): p. 229-39.
- Borrey, D., et al., **Enzymatic hydrolysis improves the sensitivity of Emit screening for urinary benzodiazepines.** Clin Chem, 2002. 48(11): p. 2047-9.
- Berna, M., et al., **Determination of olanzapine in human blood by liquid chromatography-tandem mass spectrometry.** J Chromatogr B Analyt Technol Biomed Life Sci, 2002. 767(1): p. 163-8.
- Aebi, B., et al., **Quantitation using GC-TOF-MS: example of bromazepam.** Forensic Sci Int, 2002. 128(1-2): p. 84-9.
- Valli, A., et al., **Comprehensive drug screening by integrated use of gas chromatography/mass spectrometry and Remedi HS.** Ther Drug Monit, 2001. 23(3): p. 287-94.
- Toyo'oka, T., et al., **Determination of triazolam involving its hydroxy metabolites in hair shaft and hair root by reversed-phase liquid chromatography with electrospray ionization mass spectrometry and application to human hair analysis.** Anal Biochem, 2001. 295(2): p. 172-9.
- Soriano, T., et al., **Improved solid-phase extraction method for systematic toxicological analysis in biological fluids.** J Anal Toxicol, 2001. 25(2): p. 137-43.
- Snyder, H., et al., **Serum and urine concentrations of flunitrazepam and metabolites, after a single oral dose, by immunoassay and GC-MS.** J Anal Toxicol, 2001. 25(8): p. 699-704.
- Negrusz, A., et al., **Deposition of 7-aminoflunitrazepam and flunitrazepam in hair after a single dose of Rohypnol.** J Forensic Sci, 2001. 46(5): p. 1143-51.
- Mosaddegh, M.H., et al., **Application of solid-phase micro-extraction technology to drug screening and identification.** Ann Clin Biochem, 2001. 38(Pt 5): p. 541-7.

- Liu, Z., et al., **The simultaneous determination of diazepam and its three metabolites in dog plasma by high-performance liquid chromatography with mass spectroscopy detection.** *J Pharm Biomed Anal*, 2001. 26(2): p. 321-30.
- Frison, G., et al., **Determination of midazolam in human plasma by solid-phase microextraction and gas chromatography/mass spectrometry.** *Rapid Commun Mass Spectrom*, 2001. 15(24): p. 2497-501.
- Druid, H., P. Holmgren, and J. Ahlner, **Flunitrazepam: an evaluation of use, abuse and toxicity.** *Forensic Sci Int*, 2001. 122(2-3): p. 136-41.
- Cepanec, I., et al., **Isolation and identification of a new impurity in lorazepam substance.** *Pharmazie*, 2001. 56(11): p. 857-9.
- Borrey, D., et al., **Sensitive gas chromatographic--mass spectrometric screening of acetylated benzodiazepines.** *J Chromatogr A*, 2001. 910(1): p. 105-18.
- Borrey, D., et al., **Simultaneous determination of fifteen low-dosed benzodiazepines in human urine by solid-phase extraction and gas chromatography-mass spectrometry.** *J Chromatogr B Biomed Sci Appl*, 2001. 765(2): p. 187-97.
- Yuan, H., et al., **Automated in-tube solid-phase microextraction coupled with liquid chromatography-electrospray ionization mass spectrometry for the determination of selected benzodiazepines.** *J Anal Toxicol*, 2000. 24(8): p. 718-25.
- Xu, J., Q. Zhang, and C. Wang, **Electron impact mass spectral fragmentation of 3a,5-disubstituted 1, 3-diphenyl-3a,4,5,6-tetra-hydro-3H-1,2,4-triazolo[4,3-a][1, 5]benzo-diazepines.** *Rapid Commun Mass Spectrom*, 2000. 14(24): p. 2339-42.
- Smyth, W.F., S. McClean, and V.N. Ramachandran, **A study of the electrospray ionisation of pharmacologically significant 1,4-benzodiazepines and their subsequent fragmentation using an ion-trap mass spectrometer.** *Rapid Commun Mass Spectrom*, 2000. 14(21): p. 2061-9.
- Negrusz, A., et al., **Quantitation of clonazepam and its major metabolite 7-aminoclonazepam in hair.** *J Anal Toxicol*, 2000. 24(7): p. 614-20.
- LeBeau, M.A., et al., **Analysis of biofluids for flunitrazepam and metabolites by electrospray liquid chromatography/mass spectrometry.** *J Forensic Sci*, 2000. 45(5): p. 1133-41.
- Inoue, H., et al., **Screening and determination of benzodiazepines in whole blood using solid-phase extraction and gas chromatography/mass spectrometry.** *Forensic Sci Int*, 2000. 113(1-3): p. 367-73.
- Zweigenbaum, J., et al., **High-throughput bioanalytical LC/MS/MS determination of benzodiazepines in human urine: 1000 samples per 12 hours.** *Anal Chem*, 1999. 71(13): p. 2294-300.
- Xia, Y.Q., D.B. Whigan, and M. Jemal, **A simple liquid-liquid extraction with hexane for low-picogram determination of drugs and their metabolites in plasma by high-performance liquid chromatography with positive ion electrospray tandem mass spectrometry.** *Rapid Commun Mass Spectrom*, 1999. 13(15): p. 1611-21.
- McClean, S., et al., **Determination of 1,4-benzodiazepines and their metabolites by capillary electrophoresis and high-performance liquid chromatography using ultraviolet and electrospray ionisation mass spectrometry.** *J Chromatogr A*, 1999. 838(1-2): p. 273-91.
- Fitzgerald, R.L., J.D. Rivera, and D.A. Herold, **Broad spectrum drug identification directly from urine, using liquid chromatography-tandem mass spectrometry.** *Clin Chem*, 1999. 45(8 Pt 1): p. 1224-34.

Balikova, M., V. Maresova, and J. Vecerkova, [**Sensitivity of GC-MS in the detection of benzodiazepines in the urine in the form of trimethylsilyl derivatives**]. Soud Lek, 1999. 44(3): p. 34-42.

Bogusz, M.J., et al., **Determination of flunitrazepam and its metabolites in blood by high-performance liquid chromatography-atmospheric pressure chemical ionization mass spectrometry**. J Chromatogr B Biomed Sci Appl, 1998. 713(2): p. 361-9.

Nedved, M.L., et al., **Characterization of benzodiazepine "combinatorial" chemical libraries by on-line immunoaffinity extraction, coupled column HPLC-ion spray mass spectrometry-tandem mass spectrometry**. Anal Chem, 1996. 68(23): p. 4228-36.

Kleinschnitz, M., M. Herderich, and P. Schreier, **Determination of 1,4-benzodiazepines by high-performance liquid chromatography-electrospray tandem mass spectrometry**. J Chromatogr B Biomed Appl, 1996. 676(1): p. 61-7.

Fitzgerald, R.L., D.A. Regin, and D.A. Herold, **Benzodiazepine analysis by negative chemical ionization gas chromatography/mass spectrometry**. J Anal Toxicol, 1993. 17(6): p. 342-7.

Verweij, A.M., P.J. Lipman, and P.G. Zweipfenning, **Quantitative liquid chromatography, thermospray/tandem mass spectrometry (LC/TSP/MS/MS) analysis of some thermolabile benzodiazepines in whole-blood**. Forensic Sci Int, 1992. 54(1): p. 67-74.

Musshoff, F. and T. Daldrup, **A rapid solid-phase extraction and HPLC/DAD procedure for the simultaneous determination and quantification of different benzodiazepines in serum, blood and post-mortem blood**. Int J Legal Med, 1992. 105(2): p. 105-9.