Research in Pharmaceutical Sciences, 2012;7(5)
School of Pharmacy and Pharmaceutical Sciences
Isfahan University of Medical Sciences
Proceeding of 13th Iranian Pharmaceutical Sciences Congress

Rapid determination of MDMA and its three metabolites: Application in ex vivo studies

B. Jamali[1,*], Y. Hosseinzadeh Ardakani[2], A. Foroumadi[3], H. Lavasani[2], F. Kobarfard[4], M.R. Rouini[2]

[1]Biopharmaceutics and Pharmacokinetics Division, Department of Pharmaceutics and Students' Scientific Research Center, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran
[2]Biopharmaceutics and Pharmacokinetics Division, Department of Pharmaceutics, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran
[3]Drug design and Development Research Center, Tehran University of Medical Sciences, Tehran, Iran
[4]Department of Medicinal Chemistry, School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Background and Aims: MDMA (3,4-methylenedioxymethamphetamine) is a potent releaser and/or reuptake inhibitor of serotonin. This compound, due to psychotropic and entactogenic effects is one of the most commonly abused illicit drugs in the world. MDMA is metabolized through two pathways: O-demethylation and N-dealkylation. O-demethylation produces the main instable metabolite (HHMA, 3,4-dihydroxyme-thamphetamine), which seems to be a cytotoxic compound that causes CYP2D6 inhibition and neurotoxicity. There is no report about HHMA determination in its free form in humans with simple analytical procedure. So, we decided to determine the MDMA and its metabolite (MDA, HMA and HHMA) besides MDEA (as internal standard) through HPLC with florescence detector which has the reasonable sensitivity and price.
Methods: The separation of analytes was done on the Chromolith C18 (100 × 4.6 mm) column from Merck (Darmstadt, Germany) without any derivatization. The mobile phase was a mixture of potassium dihydrogen phosphate 0.02M, pH=3 and acetonitrile (95:5) which was pumped at 1.5 mL/min in isocratic mode. The detector wavelength was fixed at 285 nm for excitation and 320 nm for emission.
Results: The data shows that this method can determine MDMA and its main metabolite as a free form as well as MDA, HMA and MDEA in water and perfusion medium. The stability, accuracy, precision and linearity of this method were determined according to FDA bioanalytical method validation guideline. The elution order was HHMA, HMA, MDA, MDMA and IS with a retention time of 1.7, 2.6, 6.1, 7.4 and 10.8 min, respectively. The obtained LOQ for MDMA, MDA, HMA and HHMA was 1, 1, 1.5 and 5 ng/mL, respectively. This method can separate these compounds in about 8 minutes without any labeling agent.
Conclusions: To our knowledge, this is the first method introduced for determination of HHMA as a free form with FL detector.

Keywords: HPLC/FL; MDMA; HHMA; MDA; HMA