Detection and validated quantification of nine herbal phenalkylamines and methcathinone in human blood plasma by LC-MS/MS with electrospray ionization

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The herbal stimulants Ephedra species, Catha edulis (khat), and Lophophora williamsii (peyote) have been abused for a long time. In recent years, the herbal drug market has grown owing to publicity on the Internet. Some ingredients of these plants are also ingredients of cold remedies. The aim of the presented study is to develop a multianalyte procedure for detection and validated quantification of the phenalkylamines ephedrine, pseudoephedrine, norephedrine, norpseudoephedrine, methylephedrine, methylpseudoephedrine, cathinone, mescaline, synephrine (oxedrine), and methcathinone in plasma. After mixed-mode solid-phase extraction of 1 ml of plasma, the analytes were separated using a strong cation exchange separation column and gradient elution. They were detected using a Q-Trap LC-ESI-MS/MS system (MRM mode). Calibration curves were used for quantification using norephedrine-d3, ephedrine-d3, and mescaline-d9 as internal standards. The method was validated according to international guidelines. The assay was selective for the tested compounds. It was linear from 10 to 1000 ng/ml for all analytes. The recoveries were generally higher than 70%. Accuracy ranged from -0.8 to 20.0%, repeatability from 2.5 to 12.3%, and intermediate precision from 4.6 to 20.0%. The lower limit of quantification was 10 ng/ml for all analytes. No instability was observed after repeated freezing and thawing or in processed samples. The applicability of the assay was tested by analysis of authentic plasma samples after ingestion of different cold medications containing ephedrine or pseudoephedrine, and after ingestion of an aqueous extract of Herba Ephedra. After ingestion of the cold medications, only the corresponding single alkaloids were detected in human plasma, whereas after ingestion of the herb extract, all six ephedrines contained in the plant were detected. The presented LC-MS/MS assay was found applicable for sensitive detection and accurate and precise quantification of all studied analytes in plasma.