Screening procedure for detection of diuretics and uricosurics and/or their metabolites in human urine using gas chromatography-mass spectrometry after extractive methylation

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A gas chromatography-mass spectrometry (GC-MS)-based screening procedure was developed for the detection of diuretics, uricosurics, and/or their metabolites in human urine after extractive methylation. Phase-transfer catalyst remaining in the organic phase was removed by solid-phase extraction on a diol phase. The compounds were separated by GC and identified by MS in the full-scan mode. The possible presence of the following drugs and/or their metabolites could be indicated using mass chromatography with the given ions: m/z 267, 352, 353, 355, 386, and 392 for thiazide diuretics bemetizide, bendroflumethiazide, butizide, chlorothiazide, cyclopenthiazide, cyclothiazide, hydrochlorothiazide, metolazone, polythiazide, and for canrenoic acid and spironolactone; m/z 77, 81, 181, 261, 270, 295, 406, and 438 for loop diuretics bumetanide, ethacrynic acid, furosemide, piretanide, torasemide, as well as the uricosurics benzbromarone, probenecid, and sulfipyrazone; m/z 84, 85, 111, 112, 135, 161, 249, 253, 289, and 363 for the other diuretics acetazolamide, carzenide, chlorothalidone, clopamide, diclofenamide, etozoline, indapamide, mefruside, tienilic acid, and xipamide. The identity of positive signals in such mass chromatograms was confirmed by comparison of the peaks underlying full mass spectra with reference spectra. This method allowed the detection of the abovementioned drugs and/or their metabolites in human urine samples, except torasemide. The limits of detection ranged from 0.001 to 5 mg/L in the full-scan mode. Recoveries of selected diuretics and uricosurics, representing the different chemical classes, ranged from 46% to 99% with coefficients of variation of less than 21%. After ingestion of the lowest therapeutic doses, furosemide was detectable in urine samples for 67 hours, hydrochlorothiazide for 48 hours, and spironolactone for 52 hours (via its target analyte canrenone). The procedure described here is part of a systematic toxicological analysis procedure for acidic drugs and poisons.