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Analysis of smoking behavior on the pharmacokinetics of antidepressants and antipsychotics: Evidence for the role of alternative pathways apart from CYP1A2

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1. AMI/NOR and DOX/N-DOX

HPLC was performed using Agilent (Santa Clara, CA, USA) 1100 and 1200 series HPLC systems. Serum concentrations of AMI/NOR and DOX/N-DOX were quantified using an isocratic reversed-phase high performance liquid chromatography (RP-HPLC) method with UV-absorbance detection. Sample cleanup was performed with online SPE for 4 minutes (MZ-PerfectBond CN 20 µm, MZ-Analysentechnik, Mainz, Germany). Afterwards the sample was transferred to the analytical column (MN-EC 150/4.6 Nucleodur 100-3 CN-RP Macherey–Nagel, Düren, Germany) by automated column switching for chromatographic separation of the target drugs. Column temperature was 30 °C and flow rate was set to 1 mL/min. For sample cleanup the mobile phase contained 10 % acetonitrile and 90 % aqua destillata, the analytical phase contained 45 % acetonitrile and 55 % 10 mM dipotassium hydrogen phosphate adjusted to a pH of 6.4 using orthophosphoric acid. For AMI/NOR and DOX/N-DOX wavelength was set at 210 nm. Retention times were as follows: amitriptyline 14.25 min, nortriptyline 13.04 min, doxepin 11.55 min and nordoxepin 10.74 min.

2. MIRT and VEN/ODM

HPLC was performed using Agilent (Santa Clara, CA, USA) 1100 and 1200 series HPLC systems. Serum concentrations of MIRT and VEN/ODM were quantified using an isocratic reversed-phase high performance liquid chromatography (RP-HPLC) method with fluorescence detection. Sample cleanup was performed with online SPE for 4 minutes (MZ-PerfectBond CN 20 µm, MZ-Analysentechnik, Mainz, Germany). Afterwards the sample was transferred to the analytical column (MN-EC 150/4.6 Nucleodur 100-3 CN-RP Macherey–Nagel, Düren, Germany) by automated column switching for chromatographic separation of the target drugs. Column temperature was 30 °C; flow rate was set to 0.75 mL/min. For sample cleanup the mobile phase contained 5 % acetonitrile and 95 % aqua destillata, the analytical phase contained 15 % acetonitrile and 85 % aqua distillata with 0.09 % trimethylamine adjusted to a pH of 2.5 using orthophosphoric acid. For MIRT extinction wavelength was set at 290 nm and emission detection wavelength at 350 nm, for VEN/ODM at 220 nm and 305 nm respectively. Retention times were as follows: mirtazapine 8.36 min, venlafaxine 11.44 min and ODM-venlafaxine 8.95 min.

3. CLOZ/N-CLOZ, QUET and RISP/9-OH

HPLC was performed using Agilent (Santa Clara, CA, USA) 1100 and 1200 series HPLC systems. Serum concentrations of CLOZ/N-CLOZ, QUET and RISP/9-OH were determined using an isocratic RP-HPLC method with UV-absorbance detection. Sample cleanup was performed with online SPE for 4 minutes (CLOZ/N-CLOZ, RISP/9-OH) and 3 minutes (QUET), respectively (MZ-PerfectBond C8 20 µm, MZ-Analysentechnik, Mainz, Germany). Afterwards the sample was transferred to the analytical column (MN-EC 150/4.6 Nucleosil 100-3 C18 HD, Macherey–Nagel, Düren, Germany) by automated column switching for chromatographic separation of the target drugs. Column temperature was 30 °C for CLOZ/N-CLOZ and RISP/9-OH and 40 °C for QUET, respectively. Flow rate was set to 1.25 mL/min for CLOZ/N-CLOZ and RISP/9-OH and to 1.5 mL/min for QUET. Mobile phase for cleanup contained 10 % acetonitrile and 90 % aqua destillata, the analytical phase contained 35 % acetonitrile and 65 % aqua destillata with 0.4 % tetramethylethylendiamin (TEMED) adjusted to a pH of 6.3 using acetic acid. Wavelength was set at 242 nm for CLOZ/N-CLOZ, at 261 nm for QUET and at 280 nm for RISP/9-OH. Retention times were as follows: clozapine 13.04 min, N-desmethylclozapine 10.15 min, quetiapine 13.83 min, risperidone 7.83 min and 9-OH-risperidone 6.97 min.