

Data Supplement

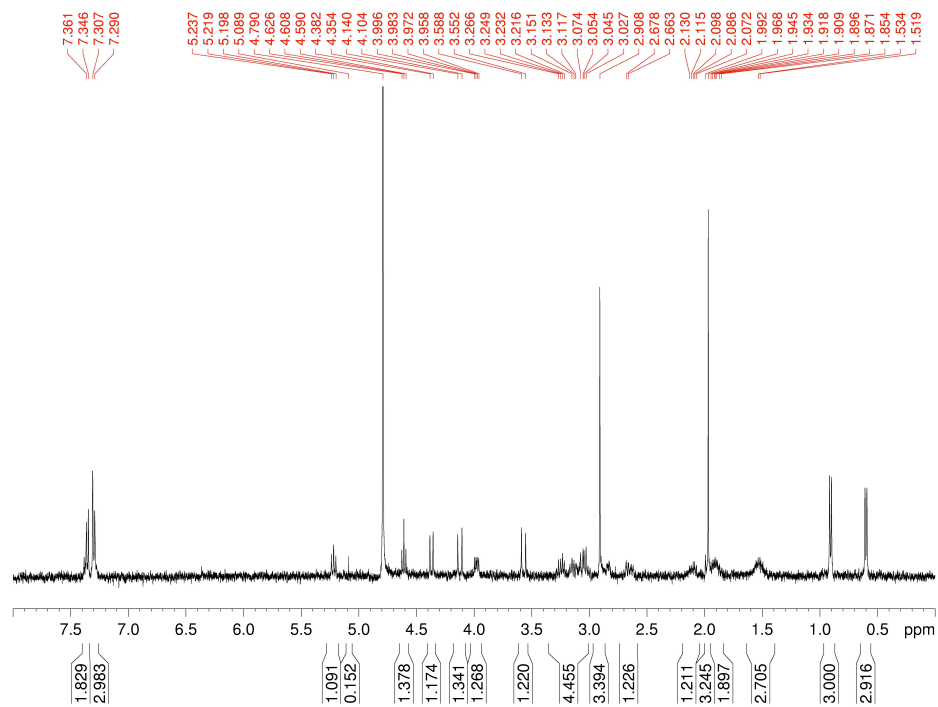
Time- and NADPH-Dependent Inhibition of P450 3A4 by the Cyclopentapeptide Cilengitide: Significance of the Guanidine Group and Accompanying Spectral Changes

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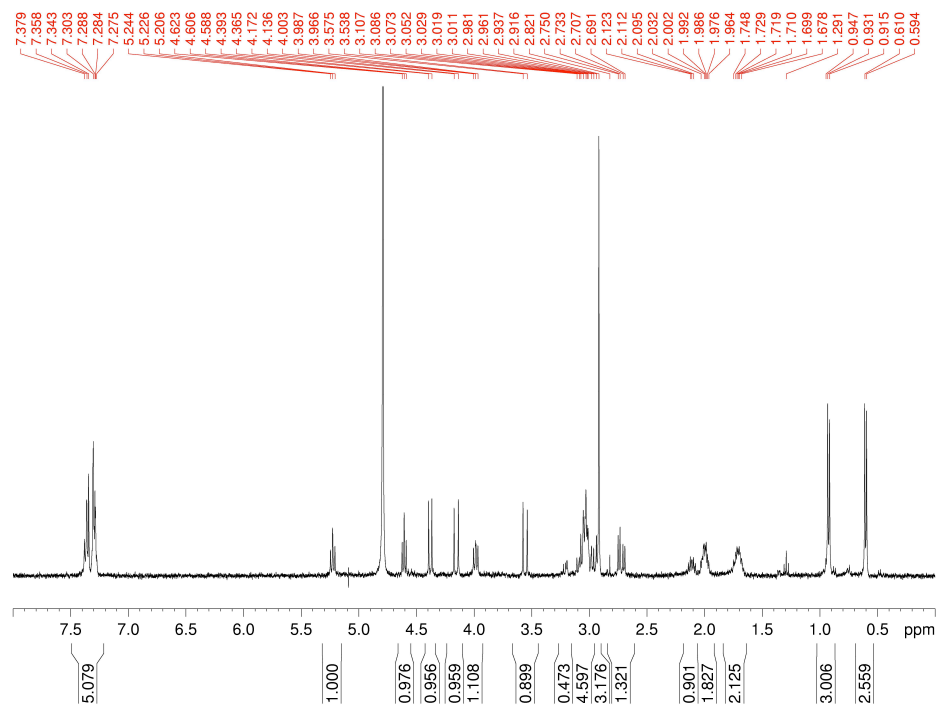
Drug Metabolism and Disposition

Fig. S1. NMR and MS data of acetylated ornithine analogue of cilengitide. (A) NMR spectra were recorded on a Bruker AV400 (400 MHz) spectrometer (Bruker AXS Inc., Madison, WI). ^1H NMR (D_2O , 400 MHz) showed a characteristic peak at δ 1.96 (s, 3H) that corresponds to the acetyl group, compared to the ornithine analogue of cilengitide (B). LC-MS analysis was performed on an Acquity UPLC (Waters, Milford, MA) coupled with an LTQ Orbitrap XL (Thermo Fisher Scientific, Waltham, MA). Separation was achieved on an Acquity UPLC BEH octadecylsilane (C_{18}) column (1.7 μm , 2.1 \times 100 mm, Waters) with H_2O and CH_3OH as the mobile phase (flow: 0.3 ml/min, gradient: 0 min, 0% CH_3OH ; 1 min, 0% CH_3OH ; 4 min, 100% CH_3OH ; 5.2 min, 100% CH_3OH ; 5.3 min, 0% CH_3OH ; 8 min, 0% CH_3OH). Mass spectrometry of the acetylated ornithine derivative in ESI positive mode (C) showed a peak ion at m/z 589 (M^+) that corresponds to the parent compound (calculated 589.2979, found 589.2980, Δ 0.2 ppm) vs. m/z 547 (M^+), which corresponds to the most intensive parent ion of the ornithine analogue (calculated 547.2875, found 547.2869, Δ 1.1 ppm).

A

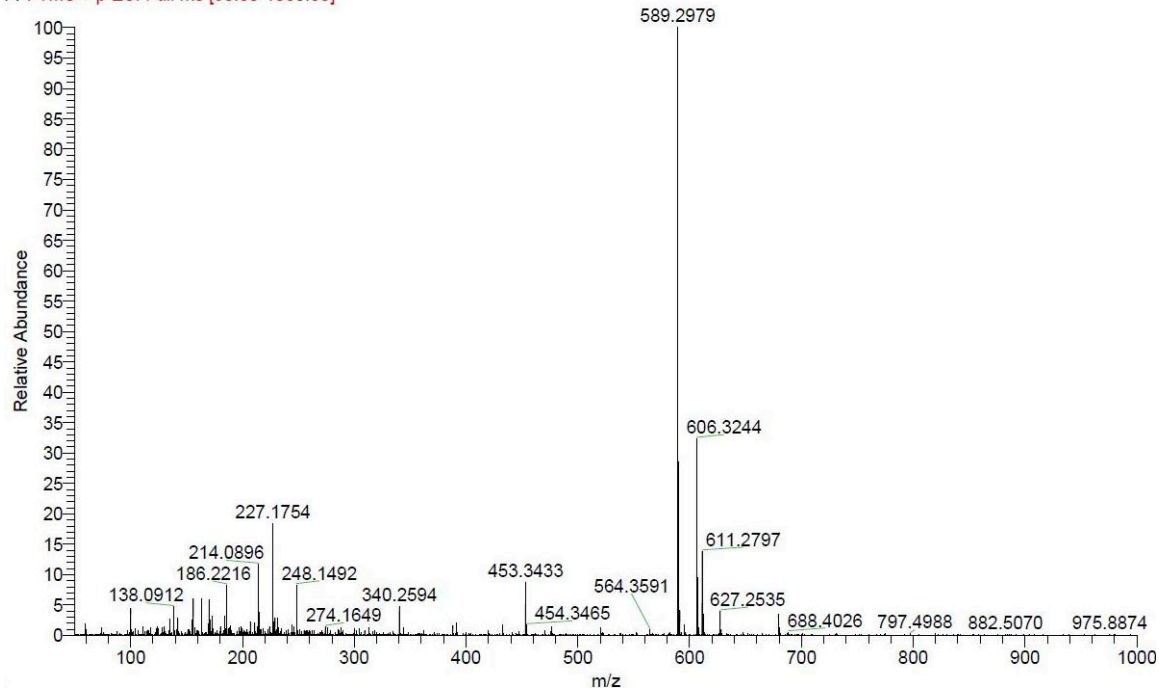


B



C

MB_acetylated_ornithine_cilengitide_10uM_5uL_injxn_12_16_2013 #55 RT: 4.33 AV: 1 NL: 5.93E6
F: FTMS + p ESI Full ms [50.00-1000.00]



D

MB_ornithine_cilengitide_10uM_5uL_injxn_12_16_2013 #50 RT: 3.97 AV: 1 NL: 2.75E6
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