Supporting Information Available: Validation data of LC/MS/MS methods used for quantitative analysis of ZP-CoA, ZP-Gly and ZP-Tau.

ZP-CoA

Calibration curves consisted of five calibration standards (n=3 at each level) and the correlation coefficients (r^2) were at least 0.990. The limit of quantification of this method was 0.01 µM and the repeatability, measured as the relative standard deviation of ZP-CoA dissolved in sample matrix (0.050 µM, n=6), was 6.6% (hepatocyte suspension) and 4.3% (liver homogenate). To assess the effect of matrix on the accuracy of rat livers analysis, ZP-CoA was dissolved in water (n=6, RSD was 9.1%) and to sample matrix (see above), and a comparison showed that the ion suppression, expressed as the ratio of: (the mean of the signal in matrix) / (the mean of the signal in water), was 1.01.

ZP-Gly and ZP-Tau

All calibration curves consisted of five standards and correlation coefficients (r^2) were at least 0.990. The quantification limits for ZP-Tau and ZP-Gly was 0.070 µM and 0.010 µM, respectively. The repeatability for ZP-Tau was 10.1% in hepatocyte suspension (0.63 µM, n=6) and 10.2% in rat livers (0.12 µM, n=6). The repeatability for ZP-Gly was 12.5% in hepatocyte suspension (0.020 µM, n=8) and 11.4% for analysis of rat livers (0.067 µM, n=6). The matrix effect was investigated in liver homogenates as described for ZP-CoA and was determined to 1.02 (ZP-Tau) and 1.32 (ZP-Gly).