



Determination of Tolbutamide and Hydroxytolbutamide by LC–MS/MS in Rat and its Application to Assessment of CYP2C9 Activity

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SUMMARY. A sensitive and selective liquid chromatography–tandem mass spectrometry method (LC–MS/MS) for the determination of tolbutamide (TB) and its metabolite hydroxytolbutamide (HTB) in rat plasma was developed using carbamazepine as an internal standard. Chromatographic separation was performed by an Agilent Zorbax SB-C18 column (150 mmx2.1 mm, 3.5 μ m), using the gradient elution of 0.1 % formic acid in water and acetonitrile. Calibration plots were linear over range of 5–1000 ng/mL for TB and 10–2000 ng/mL for HTB in rat plasma. The intra- and inter-day relative standard deviations of the assay were less than 10 % for both TB and HTB. The validated method is successfully used to analyze the influence of bupropion on cytochrome P450-mediated metabolism of TB. The biotransformation rates of TB administered either separately or both simultaneously were compared in this study. The results revealed that bupropion had no significant effect on TB hydroxylation.

KEY WORDS: CYP, Hydroxytolbutamide, LC-MS/MS, Rat, Tolbutamide.

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