Determination of Tolbutamide in Rabbit Plasma by LC–MS/MS and Its Application to Pharmacokinetic Study

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SUMMARY. A sensitive and selective liquid chromatography–tandem mass spectrometry method (LC–MS/MS) for the determination of tolbutamide in rabbit plasma was developed and validated over the concentration range of 4–1000 ng mL^{-1}. After addition of bupivacaine as internal standard (IS), a simplified protein precipitation with acetonitrile was employed for the sample preparation. Chromatographic separation was performed by an Agilent Zorbax SB-C18 column (150 mm?2.1 mm, 3.5 μm). The mobile phase was acetonitrile–1% formic acid in water (50:50 v/v) delivered at a flow rate of 0.3 mL min^{-1}. The MS data acquisition was accomplished by multiple reactions monitoring (MRM) mode with positive electrospray ionization (ESI) interface. The lower limit of quantification (LLOQ) was 4 ng mL^{-1}. For interday and intra-day tests, the precision (RSD) for the entire validation was less than 10%, and the accuracy was within the 94.7% to 105.6% range. The validated method is successfully used to analyze the drug in samples of rabbit plasma for pharmacokinetic study.