Pharmacokinetic and Bioavailability Study of Alogliptin in Rat Plasma by UPLC-MS/MS

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SUMMARY. Alogliptin, as dipeptidyl peptidase (DPP-4) inhibitor, is used for Type 2 diabetes mellitus in many counties worldwide. In this work, a sensitive and selective ultra performance liquid chromatography-tandem mass spectrometry (UPLC-MS/MS) method for determination of alogliptin in rat plasma was developed and validated. After addition of diazepam as an internal standard (IS), protein precipitation by acetonitrile-methanol (9:1, v/v) was used to prepare samples. Chromatographic separation was achieved on a UPLC BEH C18 column (2.1 × 100 mm, 1.7 μm) with 0.1% formic acid and acetonitrile as the mobile phase with gradient elution. An electrospray ionization source was applied and operated in positive ion mode; multiple reactions monitoring (MRM) mode was used for quantification using target fragment ions m/z 340.2→116.0 for alogliptin, and m/z 285.1→193.1 for IS. Calibration plots were linear throughout the range 2-2000 ng/mL for alogliptin in rat plasma. Mean recoveries of alogliptin in rat plasma ranged from 81.5% to 91.4%, matrix effect of alogliptin in rat plasma ranged from 105.9 to 110.5%. RSD of intra-day and inter-day precision were both <10%. The accuracy of the method was between 95.2% and 110.3%. The method was successfully applied to pharmacokinetic study of alogliptin after either oral or intravenous administration. The absolute bioavailability of alogliptin was reported as high as 30.9%.

KEY WORDS: alogliptin, pharmacokinetics, rat, UPLC-MS/MS.

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