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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%.**

RESUMEN. Alogliptina, como inhibidor de la dipeptidil peptidasa (DPP-4), se utiliza para la diabetes mellitus tipo 2 en todo el mundo. En este trabajo fue desarrollado y validado un método sensible y selectivo de ultra cromatografía líquida en tándem con espectrometría de masas (UPLC-MS/MS) para la determinación de alogliptina en plasma de rata. Después de la adición de diazepam como estándar interno (IS), se usó la precipitación de proteínas por acetonitrilo-metanol (9:1, *v/v*) para preparar las muestras. La separación cromatográfica se logró en una columna de UPLC BEH C18 (2,1 × 100 mm, 1,7 μm) con 0,1% de ácido fórmico y acetonitrilo como fase móvil, con gradiente de elución. Se aplicó una fuente de ionización por electrospray operada en el modo de ion positivo; para la cuantificación se usó el modo de supervisión de múltiples reacciones (MRM), utilizando iones fragmento diana *m/z* 340,2→116,0 para alogliptina y *m/z* 285,1→193,1 para IS. Los gráficos de calibración fueron lineales en todo el rango de 2-2000 ng/mL para alogliptina en plasma de rata. Las recuperaciones medias de alogliptina en plasma de rata oscilaron entre el 81,5% y el 91,4%; el efecto de la matriz de alogliptina en plasma de rata osciló entre 105,9 y 110,5%. La precisión RSD intra-día y entre días fueron ambos < 10%. La precisión del método estuvo entre 95,2 y 110,3%. El método se aplicó con éxito al estudio farmacocinético de alogliptina después de la administración oral o intravenosa. La biodisponibilidad absoluta de alogliptina resultó ser del 30,9%.

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

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