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Tissue Distribution and Pharmacokinetics of Chidamide Based on UPLC-MS/MS

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***SUMMARY*. Chidamide (epidaza) is a new oral isotype-selective HDACi (selectively inhibiting HDAC1, 2, 3 and 10) drug which belongs to benzamide class with significant anti-tumor activities. In this study, a sensitive and selective ultra performance liquid chromatography-tandem mass spectrometry (UPLC-MS/MS) method was developed and validated for determination of chidamide in tissue and plasma. 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* 391.3→265.2 for chidamide, and *m/z* 285.1→193.1 for diazepam internal standard (IS). Based on the UPLC-MS/MS method, the tissue distribution profile of chidamide in mice and plasma pharmacokinetics in rat were studied. The results showed chidamide was absorbed through intestinal tract and distributed into tissues rapidly. The level of chidamide in kidney is highest, then followed by spleen, heart, lung, brain and liver. The concentration in brain was very low, which indicated chidamide cannot across through blood brain barrier.**

RESUMEN. Chidamide (epidaza) es un nuevo isotipo selectivo oral de inhibidor de la histona deacetilasa HDACi (inhibición selectiva de HDAC1, 2, 3 y 10) que pertenece a la clase de las benzamidas, con significativa actividad antitumoral. En este estudio 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 chidamide en tejido y plasma. Se aplicó una fuente de ionización por electrospray operada en modo de iones positivos; el modo de monitorización de reacciones múltiples (MRM) se utilizó para la cuantificación usando iones fragmento diana *m/z* 391,3→265,2 para chidamide y *m/z* 285,1→193,1 para el estándar interno (IS) diazepam. Mediante método de UPLC-MS/MS fue estudiado el perfil de distribución tisular de chidamide en ratones y la farmacocinética en plasma de ratas. Los resultados mostraron que chidamide fue absorbido a través del tracto intestinal y distribuido rápidamente en los tejidos. El nivel de chidamide en riñón es el más alto, seguido por bazo, corazón, pulmones, cerebro e hígado. La concentración en el cerebro era muy baja, lo que indica que chidamide no puede pasar a través de la barrera hematoencefálica.

KEY WORDS: chidamide, pharmacokinetics, tissue distribution, UPLC-MS/MS.

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