



Determination Of Vorinostat in Rat Plasma By LC-MS and Its Application to Pharmacokinetics Study

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SUMMARY. Vorinostat, a hydroxamic acid derivative, is an analogue of trichostatin A and has pan-HDACi (histone deacetylase inhibitor) effects. The US Food and Drug Administration (FDA) approved vorinostat for the treatment of relapsed or refractory cutaneous T-cell lymphoma (CTCL). A sensitive and selective liquid chromatography mass spectrometry (LC-MS) method for determination of vorinostat in rat plasma was developed. After addition of linezolid as internal standard (IS), protein precipitation by acetonitrile was used for sample preparation. Chromatographic separation was achieved on a Zorbax SB-C18 (2.1 mm × 150 mm, 5 μm) column with acetonitrile-0.1% formic acid as mobile phase with gradient elution. Electrospray ionization (ESI) source was applied and operated in positive ion mode; selective ion monitoring (SIM) mode was used for quantification using target fragment ions *m/z* 266.2 for vorinostat and *m/z* 338.7 for the IS. Calibration plots were linear over the range of 5-500 ng/mL for vorinostat in plasma. Lower limit of quantification (LLOQ) for vorinostat was 5 ng/mL. Mean recovery of vorinostat from plasma was in the range 83.9-90.6%. Coefficient of variation (CV) of intra-day and inter-day precision were both less than 15%. This method is simple and sensitive and applied successfully in pharmacokinetic research for determination of vorinostat in rat plasma.

KEY WORDS: LC-MS, Pharmacokinetics, Rat plasma, Vorinostat.

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