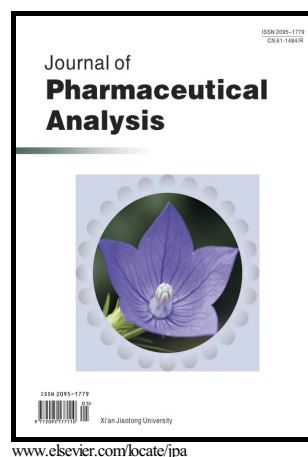


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A liquid chromatography with tandem mass spectrometry method for quantitating total and unbound ceritinib in patient plasma and brain tumor

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Abstract

A rapid, sensitive, and robust reversed-phase liquid chromatography with tandem mass spectrometry method was developed and validated for the determination of total and unbound ceritinib, a second-generation ALK inhibitor, in patient plasma and brain tumor tissue samples. Sample preparation involved simple protein precipitation with acetonitrile. Chromatographic separation was achieved on a Waters ACQUITY UPLC BEH C18 column using a 4-min gradient elution consisting of mobile phase A (0.1% formic acid in water) and mobile phase B (0.1% formic acid in acetonitrile), at a flow rate of 0.4 mL/min. Ceritinib and the internal standard ($[^{13}\text{C}_6]$ ceritinib) were monitored using multiple reaction monitoring mode under positive electrospray ionization. The lower limit of quantitation (LLOQ) was 1 nM of ceritinib in plasma. The calibration curve was linear over ceritinib concentration range of 1 – 2000 nM in plasma. The intra- and inter-day precision and accuracy were within the generally accepted criteria for bioanalytical method (< 15%). The method was successfully applied to assess ceritinib brain tumor penetration, as assessed by the unbound drug brain-to-plasma concentration ratio, in patients with brain tumors.

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