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Quantification of temozolomide in nonhuman primate fluids by Isocratic Ultra-High Performance Liquid Chromatography-Tandem Mass Spectrometry to study brain tissue penetration following intranasal or intravenous delivery

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A sensitive and selective ultra-high performance liquid chromatography-tandem mass spectrometric method was developed for the quantification of temozolomide (TMZ) in nonhuman primate (NHP) plasma, cerebrospinal fluid (CSF), and brain extracellular fluid (ECF) following microdialysis. Ethyl acetate was used to extract the plasma and CSF samples, using theophylline as the internal standard (IS). ECF samples were diluted with acetonitrile prior to analysis. TMZ was separated on a Waters UPLC® BEH C18 column with an isocratic mobile phase of ammonium acetate (10 mM)-0.1% formic acid/acetonitrile (30:70, v/v) in a positive-ion multiple reaction monitoring mode (*m/z* 195.5→137.6 for TMZ; *m/z* 181.5→124.2 for IS). The retention time of TMZ and theophylline was 0.45 min with a total run time of 2.5 min. The method was validated over the range from 5–2000 ng/mL in NHP plasma, CSF, and ECF with respect to linearity, accuracy, precision, selectivity, and stability. This method was successfully applied toward the measurement of pharmacokinetic samples following various routes of drug administration.

Biography

Peer earned his PhD in Pharmacology and Pharmaceutical Sciences in 2009, and more recently, a Masters in Pharmacometrics (2015). In 2009, he joined the Clinical Pharmacology Program at the National Cancer Institute as a postdoctoral fellow. Since 2012, Dr. Peer has been a Research Fellow and has overseen the bioanalytical operations and pharmacometric data analysis within the NCI Clinical Pharmacology Program. Dr. Peer has authored more than a dozen novel bioanalytical methods and contributed pharmacometric analyses to 24 additional publications. Dr. Peer's research interests include bioanalytical chemistry, drug metabolism and transport, PK/PD modeling and simulation, pharmacogenomics, and pharmacometric analyses.

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