VALIDATED BIOANALYTICAL METHOD

Bioanalytics, Metabolomics and Pharmacokinetics Shared Resource (BMPK)

Director: Dr. James Mohler

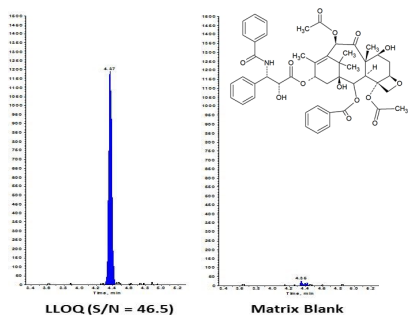
Paclitaxel in Heparinized Human Plasma

(Sensitivity: 2.00 ng/mL)

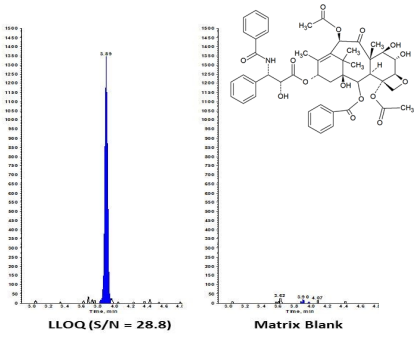
BMPK has validated a highly sensitive liquid chromatographic tandem mass spectral assay (LC-MS/MS) for the analysis of paclitaxel (TAXOL®) and its active metabolite, 6α-hydroxyl paclitaxel in heparinized plasma. Paclitaxel is a novel anti-microtubule agent that prevents microtubule disassembly and reorganization into a network essential for mitotic cellular function.[1] Currently, paclitaxel is approved alone or in combination with other chemotherapeutic agents for a variety of disease types. The validated method has been used to support a clinical trial conducted at Roswell Park Comprehensive Cancer Center entitled "*Phase I Study of Ceritinib (LDK378), a Novel ALK Inhibitor, in Combination with Gemcitabine-Based Chemotherapy in Patients with Advanced Solid Tumors*".

Specifications and Validation Performance	
Matrix (Anticoagulant):	Human Plasma (Sodium Heparin)
Required Volume:	100 µL
Preparation Procedure:	Liquid/Liquid Extraction
HPLC Column:	C18
Mobile Phase:	Acetonitrile/Methanol with Acetic Acid
Flow Rate:	400 µL/min
Detection Type:	Tandem Mass Spectral (MS/MS)
Calibration Ranges:	2.00 - 1,000 ng/mL for Pac and OH-Pac
Calibrator Accuracy:	100% (97.5 - 104%; n=5) for Pac 100% (96.3 - 105%; n=5) for OH-Pac
Calibrator Precision:	2.55% CV (0.924 - 4.69%; n=5) for Pac 2.95% CV (1.17 - 4.78%; n=5) for OH-Pac
QC Concentrations:	6.00, 75.0, 750 ng/mL for Pac and OH-Pac
QC Accuracy:	102% (99.6 - 105%; n=18) for Pac 101% (99.4 - 105%; n=18) for OH-Pac
QC Precision:	4.12% CV (2.77 - 5.12%; n=18) for Pac 3.42% CV (2.50 - 3.88%; n=18) for OH-Pac

Paclitaxel (Pac)



6α-Hydroxy Paclitaxel (OH-Pac)



Human Pharmacokinetic Parameters of Paclitaxel[1]	
Recommended Dose	100 - 175 mg/m^2 IV infusion over 1-3 hours every 2-3 weeks. Dosing is adjusted 45 - 50 mg/m^2/week depending on the disease and combination treatment.
Active Metabolite	6α-Hydroxy paclitaxel
Metabolism	CYP2C8 and CYP3A4 lead to three hydroxylated metabolites
Drug Interactions	Caution should be exercised when paclitaxel is concomitantly administered with known substrates or inhibitors of CYP2C8 and CYP3A4.
Plasma Protein Binding	89 - 98% (over the concentration range of 0.1 - 50 µg/mL)

[1]Paclitaxel Patient Information, Mylan Institutional LLC, Revised 12/2018.

BMPK offers a wide range of bioanalytical and PK/PD modeling services to assist investigators in their basic research, preclinical, and clinical study objectives. For information on services and pricing, contact John Wilton, Ph.D., Associate Director, at (716) 845-3258 or John.Wilton@RoswellPark.org.

ROSWELL PARK COMPREHENSIVE CANCER CENTER

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