Poster

# [P25-9] P25-9: Oncologic drugs (1)

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## [P25-9-2] Development and validation of a method for the determination of paclitaxel in human plasma by high performance liquid chromatography with diode array detection

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### Background

Paclitaxel is an antineoplastic drug widely used to treat different solid tumors. Despite its clinical utility, paclitaxel has a narrow therapeutic window and its use could be associated with potentially severe toxicities. Recent studies advocate therapeutic drug monitoring (TDM) of paclitaxel to ensure optimal safety and efficiency, requiring measurement of plasma concentrations about 24 h after the drug infusion. Therefore, analytical methods with adequate sensibility and specificity are mandatory to the implementation of paclitaxel TDM in the clinical setting. The aim of this study was to develop and validate a simple and fast HPLC-DAD assay for paclitaxel measurement in human plasma.

### Methods

Plasma samples (500 L) were added with 500 L ammonium acetate buffer pH 5.0, 50 L internal standard (docetaxel 2 g mL-1) and 3.5 mL of extraction solvent (acetonitrile:chlorobutane 1:4, v/v) in a microtube and homogenized. After centrifugation, an aliquot of 3 mL of the supernatant was transferred to an evaporation tube and dried at 45ºC. The dried extract was recovered with 100 L of mobile phase (acetonitrile:trietilamonium buffer pH 3.4 (42:58, v/v), flow rate 1 mL min-1) and 50 L were injected into the chromatograph. Separation was performed in a Hypersil Gold C18 column (150 x 4.6 mm, p.d. 5 m). Chromatograms were monitored at 227 nm. Evaluated validation parameters were: linearity, accuracy, intra and inter-assay precision, specificity, stability, sensibility and extraction yield

### Results

Retention times were 7.05 minutes for paclitaxel and 6.5 minutes for internal standard. The method was linear from 10 to 750 ng mL-1 (r=0.99). Extraction yield was in the range 88-90.9%. Accuracy was in the range 97-110%, while intra-assay precision was 1.29-5.59% and inter-assay precision was 3.34-9.27%. Paclitaxel was stable in plasma in three freeze/thaw cycles. The lower limit of quantification was 10 ng mL-1. No interfering peaks were detected in blank samples. The method is being applied in a clinical study evaluating genetic and pharmacokinetics contributions to paclitaxel toxicity.

### Conclusions

The developed HPLC-DAD assay is suitable for TDM of paclitaxel in the clinical setting, with sufficient sensibility to measure concentrations in plasma samples obtained about 24 after the drug infusion.