Sensitive Liquid Chromatography/Tandem Mass Spectrometry Method for the Determination of a Novel Highly Lipophilic Anti-cancer Drug Candidate in Rat Plasma and Liver Tissue
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Purpose
A simple and sensitive liquid chromatography/electrospray ionization tandem mass spectrometry (LC–ESI-MS/MS) method was developed and validated for quantification of a highly lipophilic anti-cancer drug candidate, LG1980, in rat plasma and liver tissue. LG1980 has been developed for the treatment of bone metastatic prostate cancer (PCa).

Methods
LG1980 was extracted from rat plasma and liver homogenate using liquid–liquid extraction. The compounds were separated on a Waters Atlantis™ dC-18 (30mm×2.1mm i.d., 3 μm) column using a mobile phase of acetonitrile/10mM ammonium formate/0.1 % formic acid with gradient elution. LG1980 was detected in positive ion mode using multiple reaction monitoring (MRM). The method was validated and the specificity, linearity, lower limit of quantitation (LLOQ), precision, accuracy, recoveries and stability were evaluated and met the requirements specified by the US FDA.

Results
The LLOQ was 1 ng/ml and the calibration curves proved to be linear over the concentration range from 1.0 to 200.0 ng/ml for both plasma and liver tissue. The correlation coefficient (R²) values were more than 0.995 for both plasma and liver homogenate. The precision and accuracy for intra-day and inter-day were better than 11.86 %. The relative and absolute recovery was above 112 and 60 % for plasma and liver tissue, respectively. The matrix effects were lower than 15.15 and 35.42 % for plasma and liver homogenate, respectively. This validated method has been successfully used to quantify the rat plasma and liver tissue concentration of LG1980 after chronic treatment.

Conclusion
A sensitive and robust LC-MS/MS method for simultaneous quantitation of LG1980 in rat plasma and liver homogenate, has been developed and validated for the first time. This method has been successfully applied to preclinical studies of LG1980 on rats for its anti-cancer activity research.