

Resident Research Day

College of Medicine / Department of Medical Imaging

Measurement of Gadobutrol Plasma Concentration Using Liquid Chromatography-Mass Spectroscopy as a Potential Quantification Method for Glomerular Filtration Rate

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INTRODUCTION

- Accurate monitoring of renal function is critical for the management of patients with chronic kidney disease and cancer as well as the assessment of potential live donors for kidney transplantation.
- The glomerular filtration rate (GFR) is considered the best overall measure of renal function and can be accurately determined from the plasma clearance of a single bolus injection of a glomerular filtration marker, such as; inulin, iohexol, ^{99m}Tc-DTPA, or ⁵¹Cr-EDTA.
- Contrast enhanced magnetic resonance imaging (MRI) using Gd-DTPA, a gadolinium based contrast agent (GBCA), has also been used to determine GFR, however, this method is less accurate than traditional plasma clearance techniques.
- Clinical benefit to be able to accurately determine renal function during a contrast enhanced MRI procedure.
- We propose using a GBCA as a plasma clearance marker.

OBJECTIVE

- The purpose of this study is to evaluate the possible use of mass spectroscopy as a technique to measure the plasma clearance of non-radioactive gadobutrol for determining GFR

MATERIALS & METHODS

- Gadobutrol was mixed with reconstituted bovine plasma at concentrations of 0.05, 0.01, 0.005, 0.001, 0.0005, 0.0001, 0.00005, 0.00001 mg/ml.
- Samples were then analyzed using liquid chromatography-mass spectroscopy (LC-MS) to determine the relationship between spectroscopic signal and concentration.
- Four samples of unknown concentration were also prepared by a third party and used to blindly test the accuracy of the calibration curve.

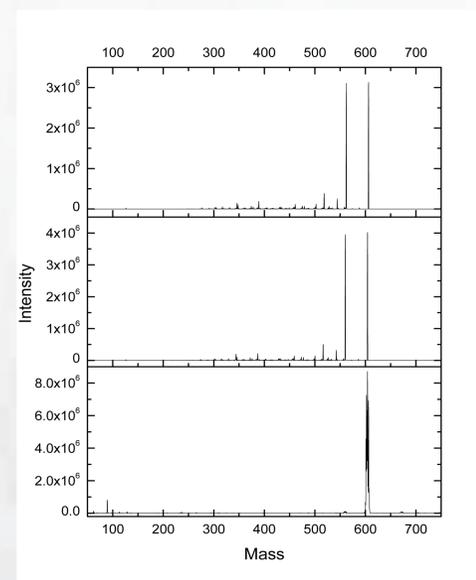


Figure 1: Mass spectrometry relationship between mass and signal intensity

RESULTS

- Using the LC-MS data a calibration curve that outlines the relationship between gadobutrol concentration and spectroscopic signature was created and was found to be linear with an $R^2 = 0.99$
- Concentrations of gadobutrol as low as 100 ng/ml can be measured accurately.
- Four samples of unknown concentration were then used to test this curve and their measured concentration values were all found to be within 10% and average of 5.2% of their true concentration values.

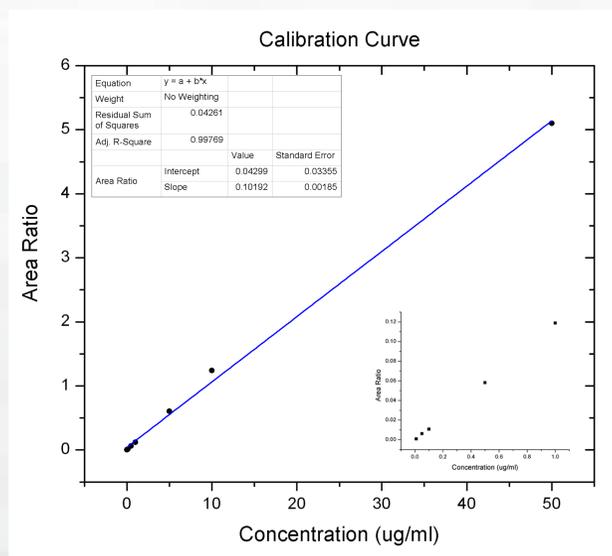


Figure 2: Calibration curve demonstrating linear relationship between gadobutrol concentration and spectroscopic signature

CONCLUSIONS

- Concentrations of gadobutrol as low as 100 ng/ml were successfully detected in the plasma samples using the LC-MS technique.
- For comparison, the typical concentration of gadobutrol in the blood of a human patient undergoing contrast enhanced MRI is on the order of mg/ml.
- The difference between the sample concentrations calculated using the calibration curve and the true concentrations of blindly prepared sample was on average 5.2%.
- This suggests that the detection of gadobutrol using LC-MS could be used to determine plasma clearance in the future.

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ACKNOWLEDGEMENTS

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