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Simplified approach for the development of a bioanalytical DBS assay using a tandem quadrupole with a novel collision cell design

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Dried blood spots (DBS) have been used for over 20 years in neonatal testing. This approach has now been applied to the field of bioanalysis in preclinical, toxicokinetic, and clinical studies. However, the small volumes typical of the DBS sample require highly-sensitive LC/MS/MS assays and the card itself can present matrix issues. Here we present the use of new UPLC/MS/MS technology for rapid method development,high sensitivity analysis of pharmaceutical compounds in DBS samples. The blood spot cards are available in two main formats, those that are treated and those that are untreated. The antiviral-anti-infective chemicals on the treated cards can, themselves, be dissolved during the extraction process and have been reported to interfere with the analyte signal. It is therefore critical during method development that the background signal from the card is monitored such that the chromatography can be adjusted to provide resolution from the analyte ion. In this study we employed a new type of tandem quadrupole MS with a novel collision cell design, allowing simultaneous collection of full scan and MRM data. The data was collected for three types of blood spot cards which had been spiked with the compound alprazolam. The data shows the untreated card exhibits a significantly lower background signal than that of the treated cards. The full scan MS data of each of the cards shows the treated cards have an increasingly intense ion current as the organic concentration of the LC gradient increases. This is also reflected in the response of analyte ion where the signal response is reduced with the treated cards compared to the untreated card. The alprazolam assay was shown to be linear over the calibration range of 100pg/mL to 500ng/mL. This UPLC/MS/MS approach was repeated for the analysis of sitamiquine from blood spots, it was possible to reach an LLOQ of 50pg/mL with a linear dynamic range of 4 orders of magnitude. The QC data shows the low concentration QCs had a RSD of 2.08 % and the highest QC a reproducibility of 3.8 %; giving confidence that a high sensitivity assays can be developed with good reproducibility.

Biography

Dr. Gopal Vaidyanathan, General Manager - Mass Spectrometry, Waters India Pvt. Ltd. Previously he worked as a Director - Analytical Research at Advinus Therapeutics- A TATA Enterprise B.Sc (Tech) in Chemical Technology (1984-1987) at University of Mumbai, India.

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