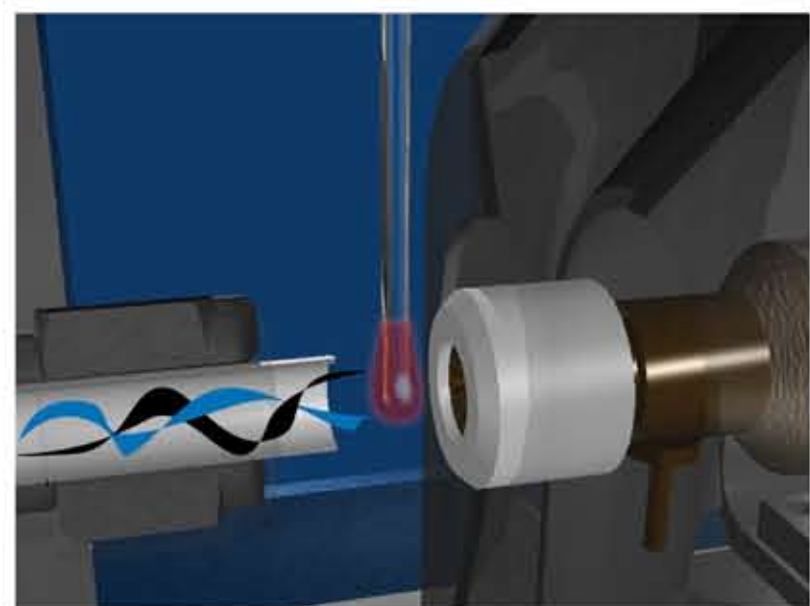


Overview

Considerably improved performance for the Direct Analysis in Real Time (DART®) experiment using the IonSense VAPUR® Technology has enabled analysis specifically of drug candidates in plasma with sub-5% CV values.

The VAPUR® Technology has been implemented on the following LC/MS systems:

- Applied Biosystems/MDS Sciex API 4000
- JEOL AccuTOF
- Finnigan LCG Deca Ion Trap



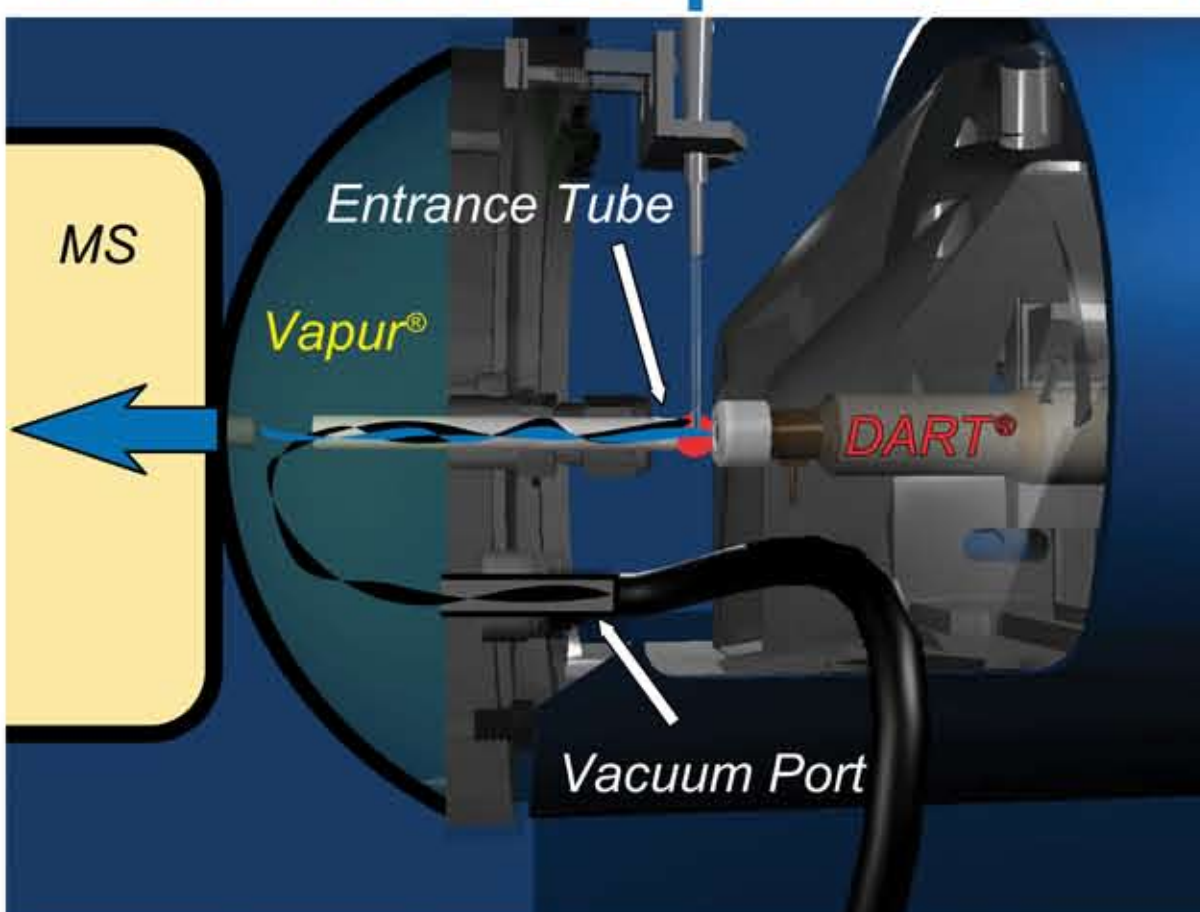
Sampling from the outer surface of a glass capillary tube

Introduction

A novel gas ion separator API interface, supported by IonSense VAPUR® Technology, has been designed to more efficiently collect and transport ions from an atmospheric pressure ionization source, such as the Direct Analysis in Real Time (DART®) source, towards the mass spectrometer's API inlet. Development and implementation of the gas ion separator interface has been performed on three different mass spectrometers for quantitative analysis: Applied Biosystems/MDS Sciex API 4000, JEOL AccuTOF and Finnigan LCG Deca Ion Trap.

While conventional implementation of surface ionization sources such as the metastable mediated desorption ionization DART® and Desorption Electrospray Ionization (DESI) can be completed with minimal redesign, the use of a more effective means to entrain ions in a larger volume of gas and transfer them into the mass spectrometer has improved performance by 100-fold when analysis of untreated samples such as plasma is completed.

Gas Ion Separator VAPUR® Technology



Technology

This figure shows a cut away side view of the gas ion separator VAPUR® Technology.

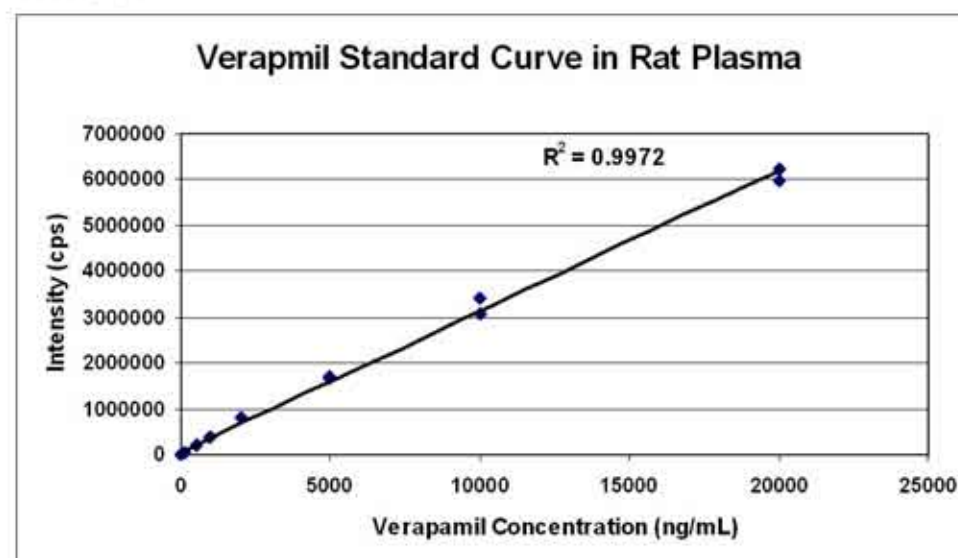
Ions created just outside of the DART® source are efficiently collected and pulled in towards the mass spectrometer's API inlet.

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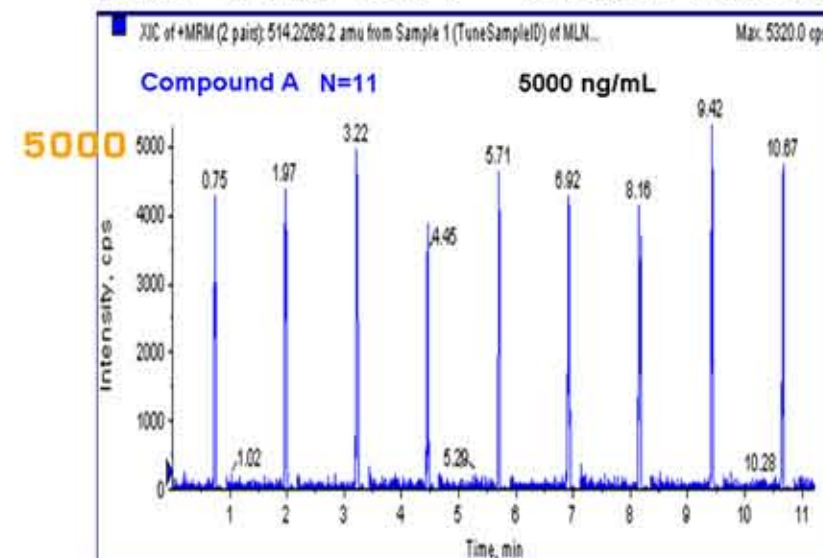
DART/API 4000 Quantitative Analyses

Challenges Faced:

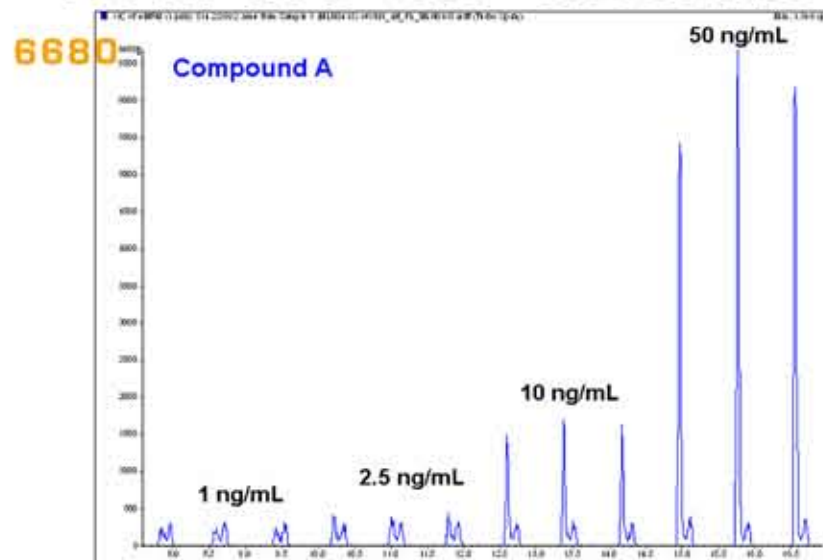
- Very poor analyte sensitivity without the VAPUR® interface.
- Poor sample to sample reproducibility.
- The API 4000 vacuum system would repeatedly shut down due to the large influx of helium gas, the more sensitive ionization gas for DART® analyses.
- High helium gas flow (4-6 L/min) was needed to push the ions through a 10 inch long ceramic transfer tube to the API inlet.



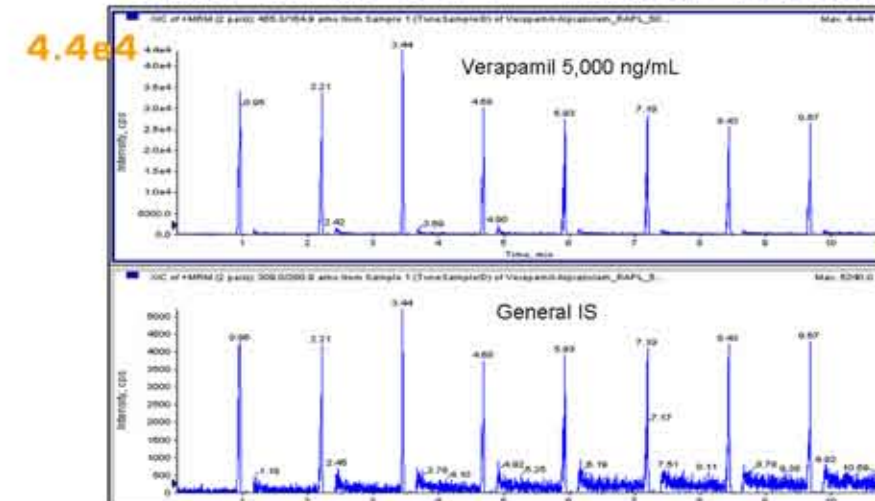
No VAPUR® Interface



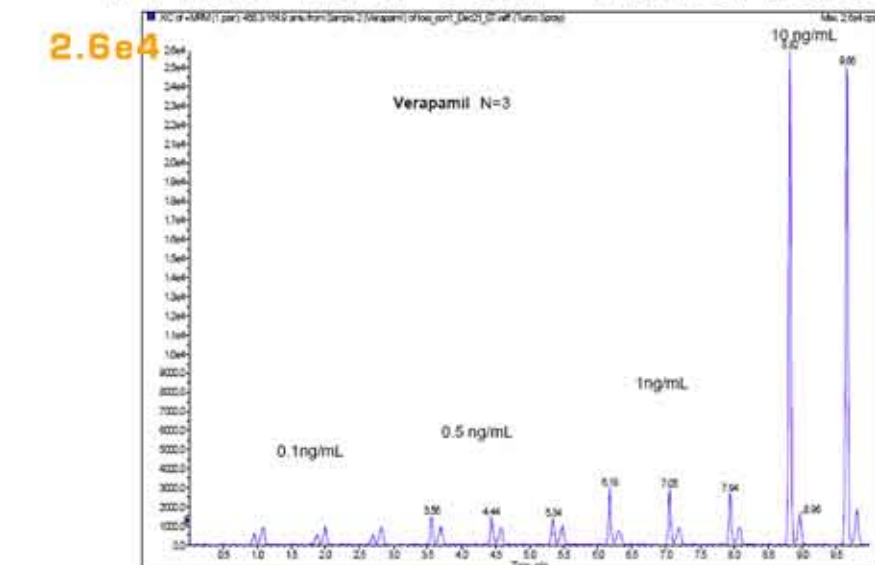
With VAPUR® Interface



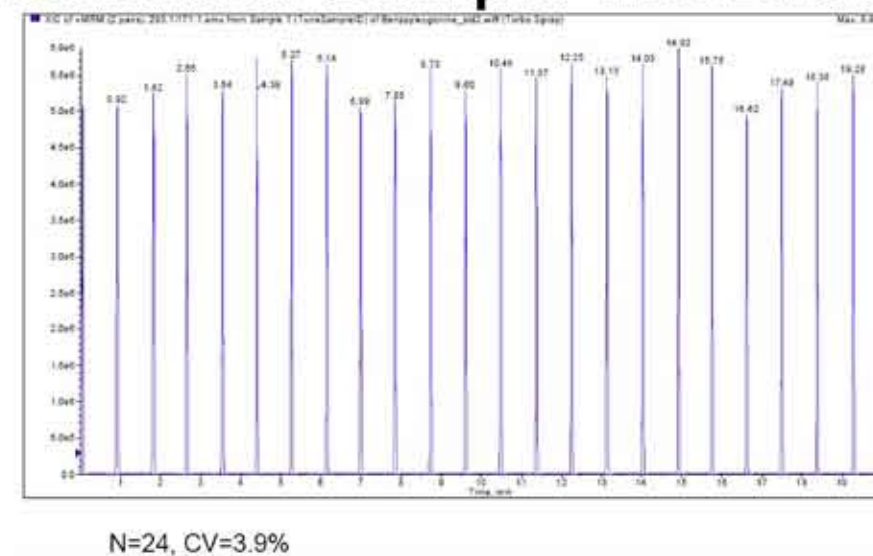
No VAPUR® Interface



With VAPUR® Interface



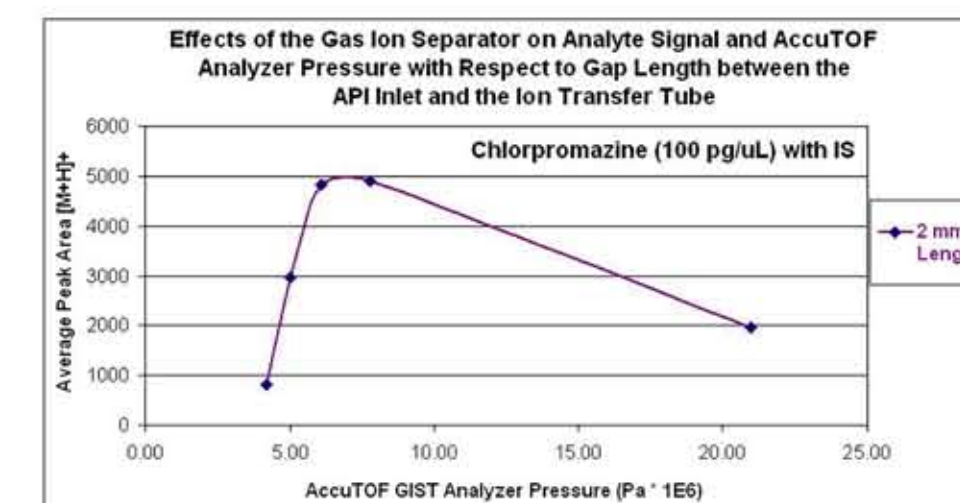
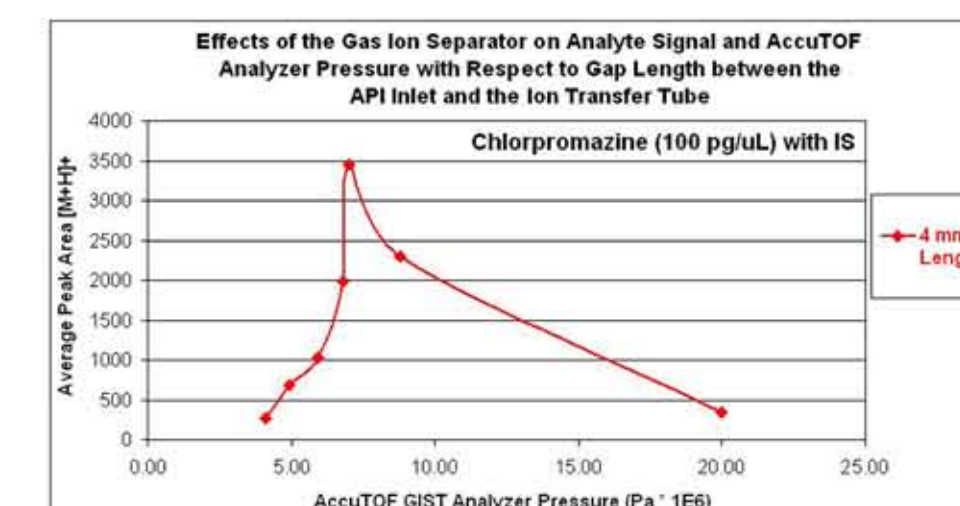
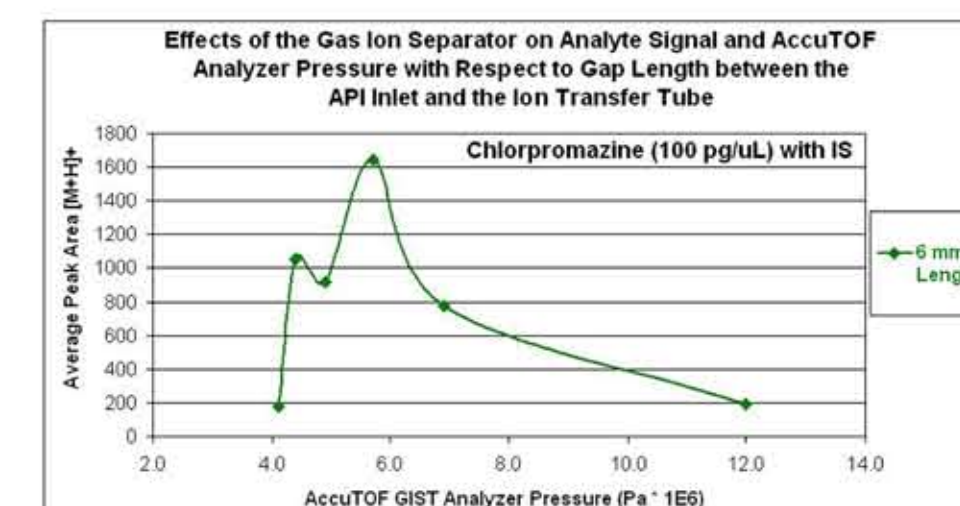
Automated Sample Introduction



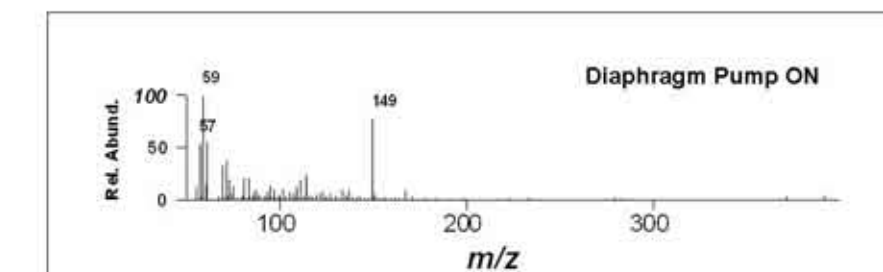
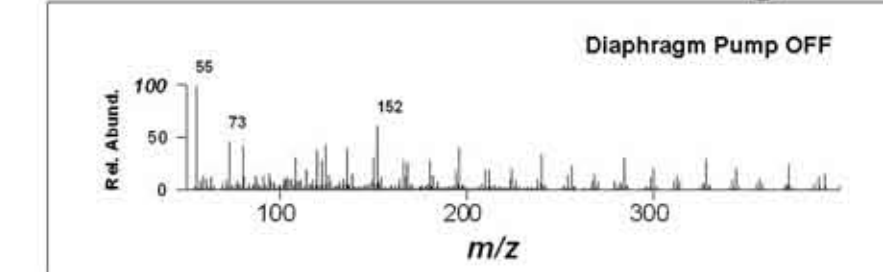
Advancements Made with the Gas Ion Separator VAPUR® Technology:

- A 100- 500 fold increase in sensitivity was observed for the API 4000 VAPUR® interface.
- Much improved sample to sample reproducibility.
- Reduced helium consumption since no longer relying on the momentum of the DART® gas to push the ions towards the API inlet, instead the gas ion separator is effectively pulling the ions towards the API inlet and therefore the helium flow can be reduced. Helium flow reduced from 4-6 L/min to 1-2 L/min.

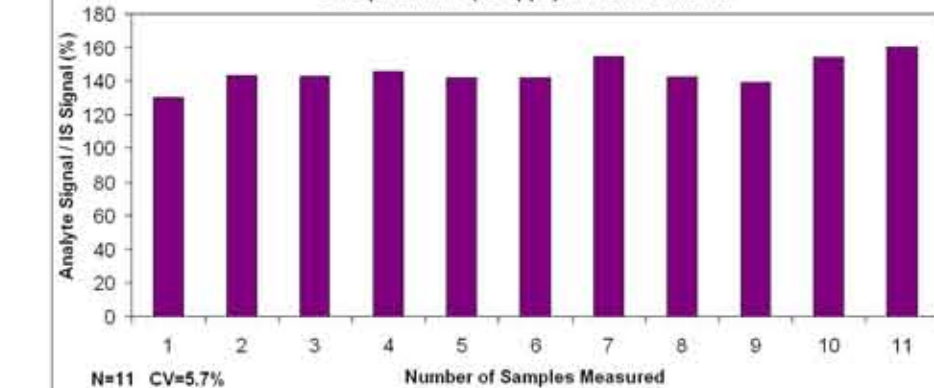
DART/AccuTOF Accurate Mass



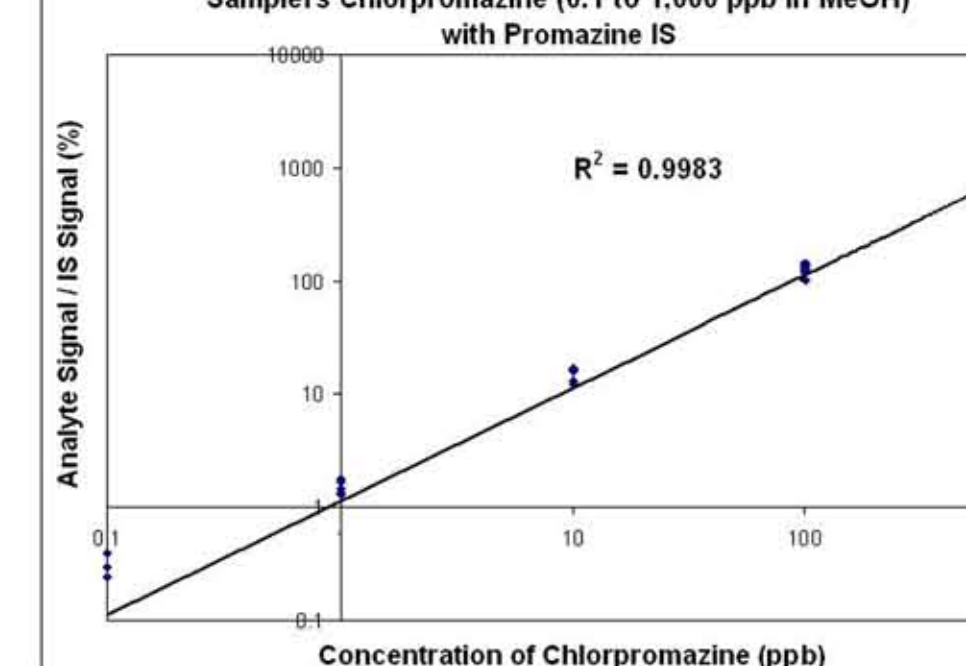
Reduction of DART® Background



Precision: Sample to Sample Reproducibility with Vapur Interface



Standard Curve: AutoDART Performance with Alumina DIP-it Samplers Chlorpromazine (0.1 to 1,000 ppb in MeOH) with Promazine IS



Conclusions

The gas ion separator VAPUR® Technology allows the DART® user to operate at significantly reduced helium flow rates, while improving overall ion transmission. The major focus of the work done on the API 4000 was quantitative analysis of raw biological samples with DART®. Implementing the VAPUR® interface on the API 4000 improved overall sensitivity for analytes directly sampled out of plasma by a factor between 100 - 500 depending on the compound.

The VAPUR® interface implemented on the JEOL AccuTOF also has allowed the DART® user to reduce the helium flow, while improving overall sensitivity.

Acknowledgments

Shaoxia Yu, Millennium Pharmaceuticals, Cambridge, MA for the API 4000 data
Dr. Chip Cody at JEOL USA for collaborating efforts on the JEOL AccuTOF
Michael Festa at IonSense, Inc. for the VAPUR® interface detailed images