Robustness and System-Health Study on Triple Quadrupole Mass Spectrometers

Mary Blackburn, Michael Belford, Jean-Jacques Dunyach, Josh Maze, Philip Remes, and Harald Oser
Thermo Fisher Scientific, San Jose, CA

Overview

Purpose: Two novel triple-quadrupole mass spectrometers with improved robustness are described.

Methods: An infusion of raw matrix was introduced to rapidly age the ion path. Once fouled, the mass spectrometer was tested for sensitivity. Any points of system charging were detected using a novel algorithm described here.

Results: Both mass spectrometers introduced here exhibited significant improvements in robustness compared to current instruments. Furthermore, any charging was detected at the specific lens of interest, allowing for quick cleaning.

Introduction

Triple-quadrupole mass spectrometers are typically considered the most sensitive mass spectrometers currently available. Current mass spectrometer market trends continue to drive limits of detection to ever lower levels. To achieve desired limits of detection, it is necessary to increase the flux of ion into the mass spectrometer. The increase in flux results not only in increased sensitivity but also increased exposure to matrix species which ultimately reduce the performance of the instrument if not mitigated. We propose the application of a new source and ion optics design that specifically addresses the increase in flux while maintaining long-term performance. In addition, we introduce a novel software/hardware routine that identifies sites of contamination, if performance declines, throughout the entire ion path.

.Methods

Sample Preparation

Samples; synthetic serum (SeraSub®), alprazolam

Liquid Chromatography

An infusion of SeraSub was teed into 62% methanol:78% water and 0.1% formic acid Isocratic elution at 500uL/min. Alprazolam data was acquired under the same chromatographic conditions.

Mass Spectrometry

Mass spec conditions; Source 3600V, vaporizer 450 ºC, sheath 40, aux 10, sweep 0, capillary 340 ºC. Acquisition parameters were Q1 and Q3 operated at a resolution of 0.7 FWHM, 309 to 281 transition monitored with a collision energy of 28 eV and CID gas pressure of 1.5 mTorr.

System Health Evaluation

Assessment of system health was performed using a novel routine. The routine identifies potential sites of contamination by selectively exposing each element in the ion path to negatively charged ions.

Data Analysis

Chromatographic peak areas were obtained using Thermo Scientific™ Xcalibur™ Quantitative Processing software. Resulting peak areas were plotted using Microsoft® Excel® software.

Results

Experimental Design

Contamination of the source is difficult to achieve in a reasonable time frame. Therefore, to mimic the effect of running a system for days or weeks with a heavy sample load, a calculated amount of undiluted SeraSub, equivalent to in excess of 5000 injections, was infused into the source while monitoring the SRM transition for alprazolam. Two different instruments were evaluated; one instrument with a standard bore capillary (0.6 mm round opening, Figure 1), the Thermo Scientific™ TSQ Endura MS, and the second with a large bore high throughput capillary (0.6 mm x 2 mm rectangular opening, Figure 1), the Thermo Scientific™ TSQ Quantiva™ triple-stage quadrupole mass spectrometer . Both systems contain identical ion-vector optics designed to prevent the passage of neutral species beyond the ion-vector region. Prior to starting experiments the “system health” routine was run to give a baseline response for a clean system, and 3 replicate alprazolam injections were performed to establish alprazolam sensitivity. Subsequent changes in sensitivity were assessed by monitoring the response of alprazolam injections between infusions of SeraSub.

Experimental Design (continued)

The setup for the infusion of the SeraSub material is depicted in Figure 2. The source position for the infusion was set to position two, which is the sprayer position closest to the ion transfer tube when the sweep cap is installed. To increase the stress on the system, the sweep gas was turned off and the source housing drain insert was removed. In this configuration the maximum amount of matrix will be introduced into the system.

The "system health" routine performs a systematic evaluation of the ion path, one element at a time, by monitoring the response of positively charged *m/z* 508 (polytyrosine) before and after exposing each element to negatively charged ions. If the element under evaluation has built up a charged layer of material, the negative ions will discharge it, altering the transmission of the positive ion signal. The change in signal identifies the element as being contaminated.

Ion Optics, Robustness and Ease of use

The Thermo Scientific™ Quantiva™ triple-stage quadrupole mass spectrometer has an RF only electrodynamic ion funnel, multipole (MP00), and lens0, shown in Figure 3. The TSQ Endura MS has the same configuration with the ion funnel being replaced by a straight RF only stacked rings ion guide (S-lens). For both systems, the multipole and the subsequent lens are the first components after the transfer tube that may require maintenance and as such are designed to be easily removed and cleaned with minimal user effort. Both systems contain the same curved ion beam guide and neutral blocking post (shown in Figure 4) that prevent the transmission of neutrals further downstream in the instrument. This component can also be easily removed for maintenance if needed.

FIGURE 1. TSQ Endura MS with 0.6 mm ion transfer tube (left) and the TSQ Quantiva MS with 0.6 mm x 2 mm High Capacity Transfer Tube (HCTT) (right).

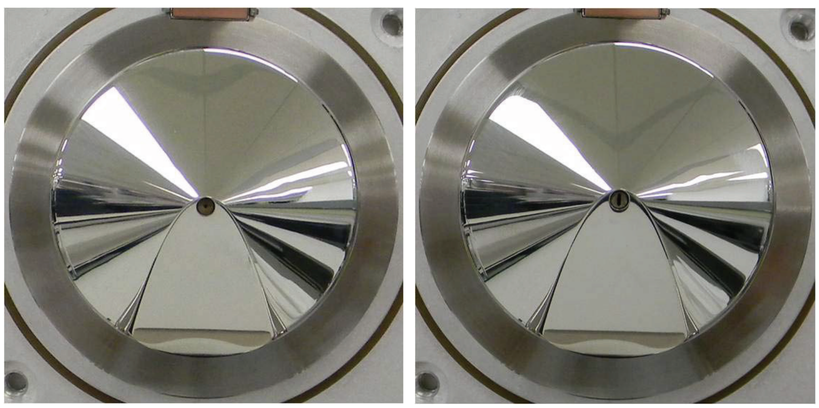


FIGURE 2. Block diagram depicting setup for robustness infusion experiment.

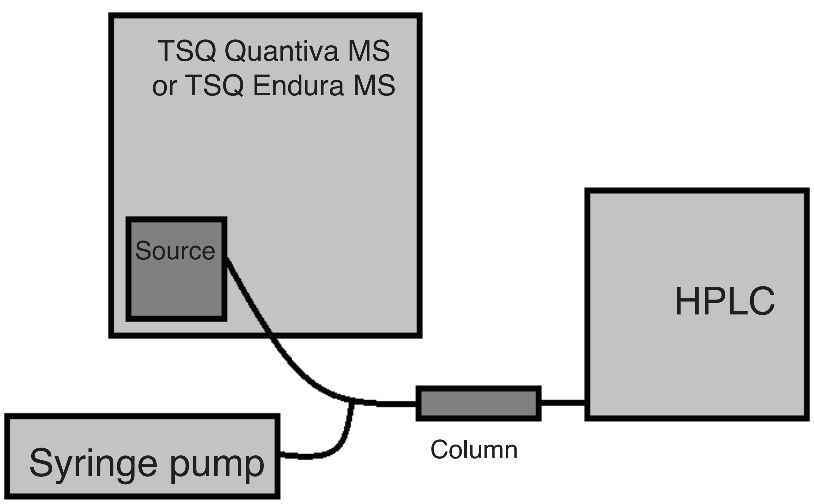


FIGURE 3. Electrodynamic ion funnel, MP00, and Lens0 devices.

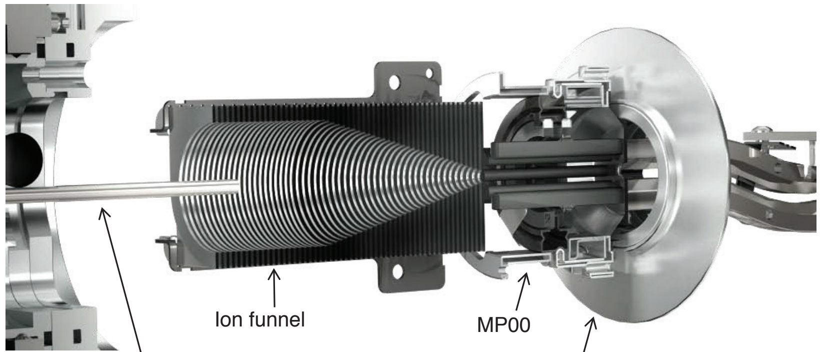
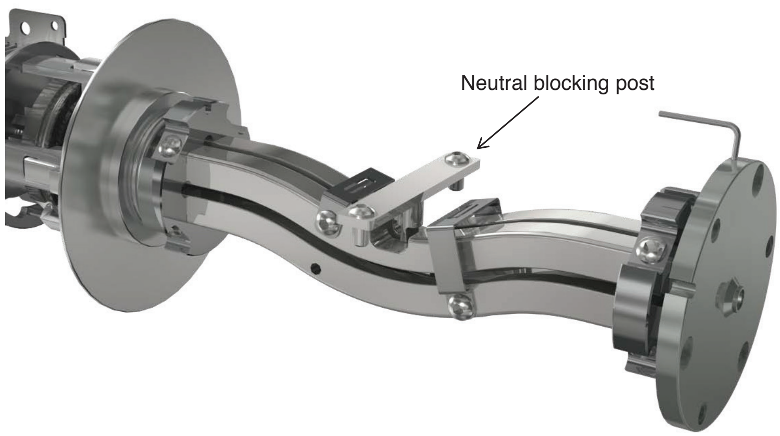


FIGURE 4. Curved ion beam guide and neutral blocking post.



System Health

The result of the system health check performed on a clean system prior to the infusion of SeraSub is shown in Figure 5. Note that for all elements in the ion path, the signal is the same before and after the discharge period. Following the system health check, SeraSub was infused into both the TSQ Endura MS and the TSQ Quantiva MS as described previously, and alprazolam measurements were made . The results of the alprazolam response at various SeraSub infusion intervals, for both systems, are shown in Figure 6. The results of the robustness test show that the alprazolam response on both the TSQ Quantiva MS and TSQ Endura MS was stable after infusion of more than 5000 μL of SeraSub. This result is compared to a triple quad equipped with a S-Lens similar to that in the TSQ Endura MS but without the improved ion optics that both the TSQ Endura MS and TSQ Quantiva MS contain. The benefit of the improved ion optics is clearly shown in the increase in robustness demonstrated in Figure 6.

As the robustness test did not result in contamination, it was necessary to artificially contaminate one of the ion optics to demonstrate the effectiveness of the system health check. The first portion of the ion beam guide was intentionally contaminated with a spot of SeraSub mixed with rhodamine dye, as shown in Figure 7. The result of the contamination is clearly shown in shown in Figure 7. The signal increases after the ion beam guide (q0) is discharged indicating that this is the site of contamination. The system health check helps to identify the site of contamination thereby facilitating cleaning of the correct element to restore system performance. The ability to diagnose the presence and location of contamination prevents needless venting in the case where the system is clean, and focuses maintenance efforts in the case where the system is contaminated.

FIGURE 5. System health test results for a clean system.

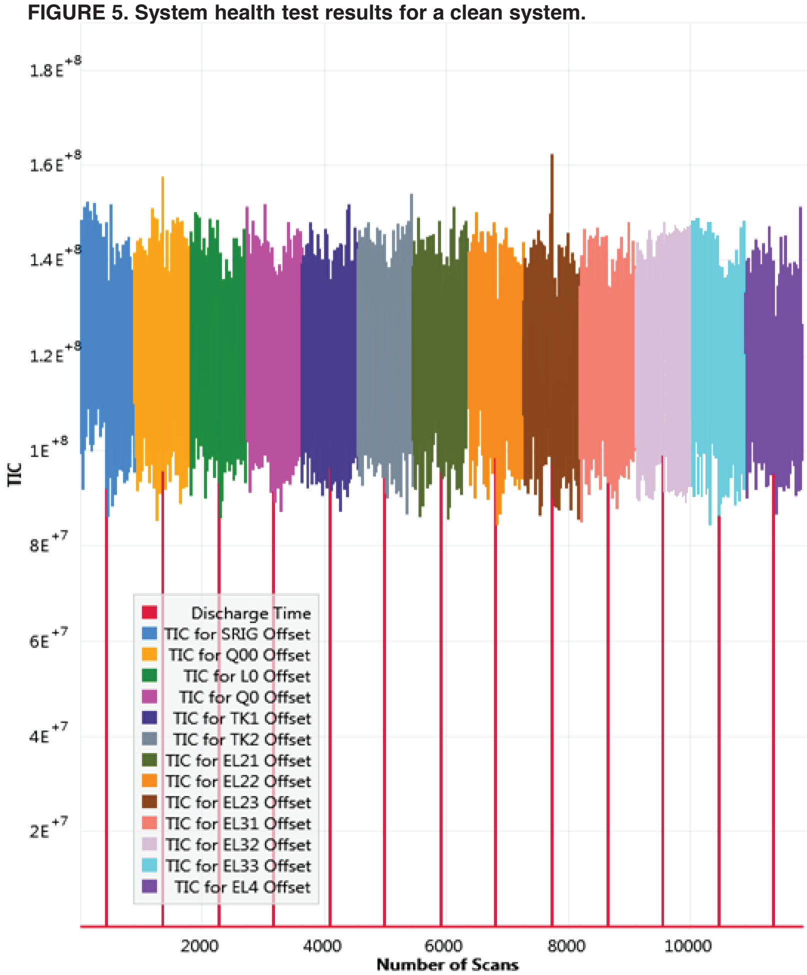


FIGURE 6. Results of robustness comparison. Normalized peak area represents the results of triplicate injections of alprazolam performed at the indicated volumes of infused SeraSub .

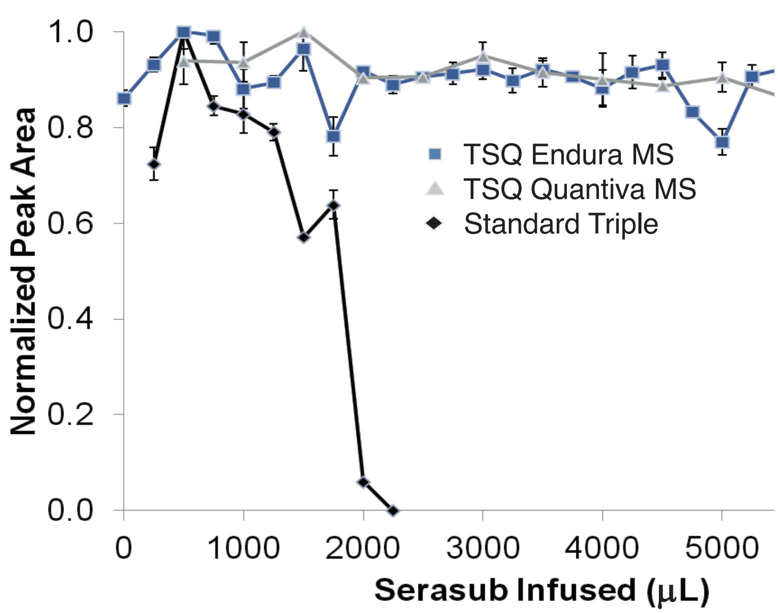
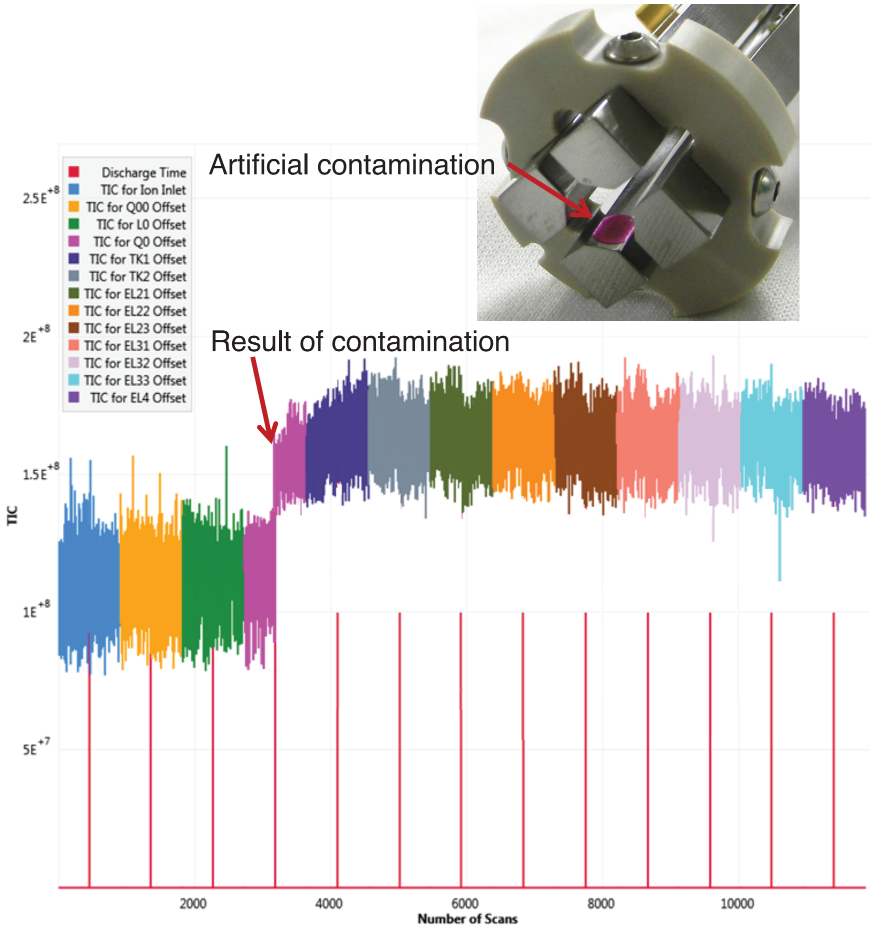


FIGURE 7. System health test results for a system intentionally contaminated in in the ion beam guide (q0) region.



Conclusion

- Two new triple-quadrupole mass spectrometers, TSQ Quantiva MS and TSQ Endura MS, are described.
- Both new instruments show improved robustness compared to a standard triple-quadrupole configuration.
- An improved source housing, with a new drain insert, reduces the amount of chemical background introduced into the system.
- A new curved multipole with neutral blocking post removes the line of sight from the source region to the mass analyzer region. This blocks neutral contaminants from being introduced downstream.
- In situations where cleaning the elements along the ion path is necessary, a novel system health routine effectively identifies the site of contamination.
- All elements in the ion path up to Q1 are easily removable without opening the high vacuum chamber allowing for easy cleaning.

www.thermoscientific.com

©2013 Thermo Fisher Scientific Inc. All rights reserved. ISO is a trademark of the International Standards Organization. Microsoft and Excel are trademarks of Microsoft Corporation. SeraSubis a trademark of CST Technologies, Inc. All other trademarks are the property of Thermo Fisher Scientific, Inc. and its subsidiaries. Specifications, terms and pricing are subject to change. Not all products are available in all countries. Please consult your local sales representative for details.

Certified System ISO 9001 QMI-SAI Global

Thermo Fisher Scientific, San Jose, CA USA is ISO 9001:2008 Certified.

Africa-Other +27 11 570 1840
Australia +61 3 9757 4300
Austria +43 1 333 50 34 0
Belgium +32 53 73 42 41
Canada +1 800 530 8447
China +86 10 8419 3588
Denmark +45 70 23 62 60
Europe-Other +43 1 333 50 34 0
Finland/Norway/Sweden +46 8 556 468 00
France +33 1 60 92 48 00
Germany +49 6103 408 1014
India +91 22 6742 9434
Italy +39 02 950 591
Japan +81 45 453 9100
Latin America +1 561 688 8700
Middle East +43 1 333 50 34 0
Netherlands +31 76 579 55 55
New Zealand +64 9 980 6700
Russia/CIS +43 1 333 50 34 0
South Africa +27 11 570 1840
Spain +34 914 845 965
Switzerland +41 61 716 77 00
UK +44 1442 233555
USA +1 800 532 4752

Thermo SCIENTIFIC

Part of Thermo Fisher Scientific

ASMS13_Th093_MBlackburn_E 07/13S