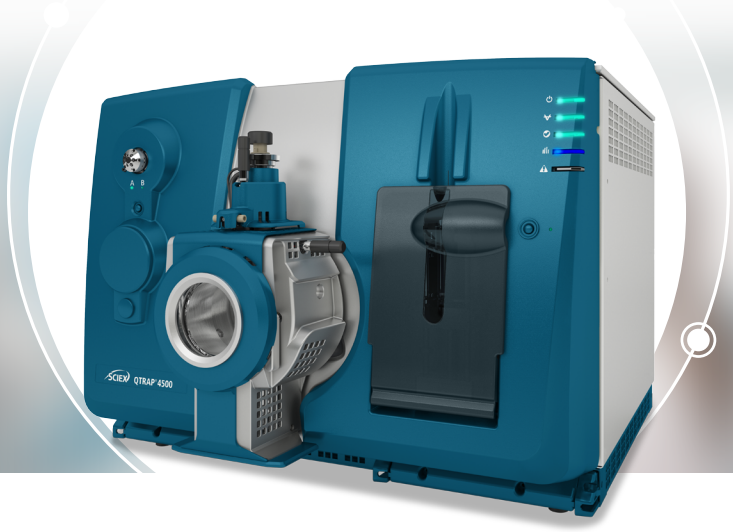
Quantify NDMA using the SCIEX QTRAP® 4500 LC-MS/MS System



N-Nitrosodimethylamine (NDMA) Analysis in Ranitidine Active Pharmaceutical Ingredient and Drug Product Using QTRAP® 4500 System

The presence of nitrosamines, especially NDMA, has been identified in ranitidine drug products by the United States Food and Drug Administration (FDA)and appropriate measures to recall some of the ranitidine drug products is underway. The products having contamination of NDMA higher than 0.09 PPM were issued a warning by the FDA.

A sensitive analytical method has been developed using the QTRAP® 4500 System for identification and quantitation of NDMA in active pharmaceutical ingredients and drug products that meets all the regulatory requirements. The LC-MS/MS is highly efficient for identification and quantitative low levels of NDMA (0.5 ng/ml or 0.01 PPM) in ranitidine API and drug products. The analytical method provides detection and quantification of the NDMA at levels much lower than regulatory limits and will prove useful for routine NDMA quantitation in quality control for API and drug products.

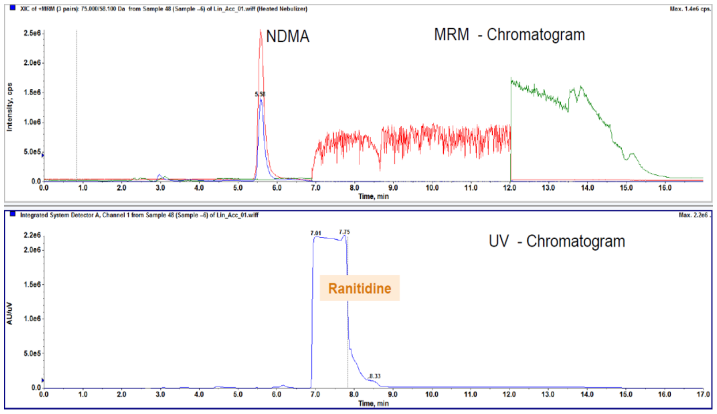


Figure 1. Chromatogram of Ranitidine sample containing NDMA contamination, upper panel showing 3 transition of MS/MS for NDMA (75>43- red, 75>58.1- blue) and Ranitidine (315.1>229.9- green), and the lower panel showing UV chromatogram with ranitidine eluting at 7.01 – 8.7 in valco waste line.

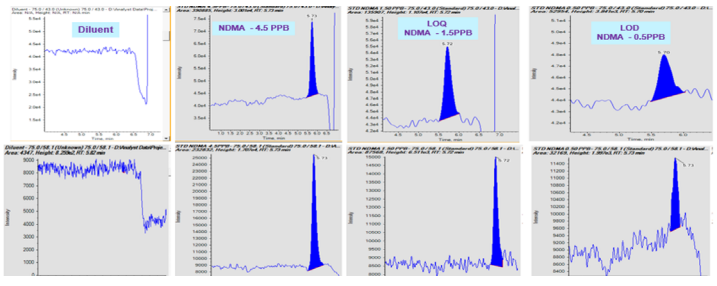


Figure 2. Extracted Ion Chromatogram of analyte at diluent, specification, LOQ and LOD level.

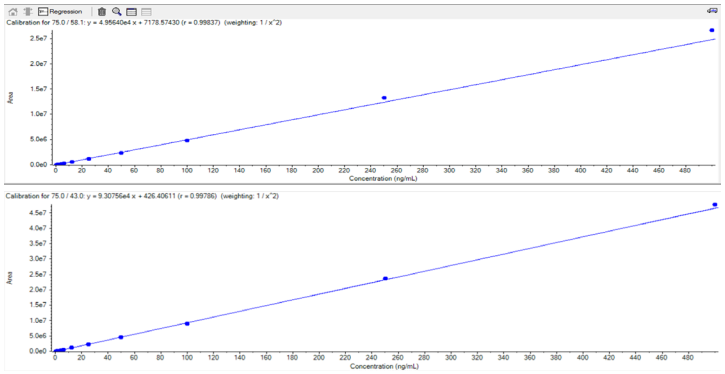


Figure 3. : Calibration Curve for NDMA with calibration range 0.5ng/ml to 500ng/ml for both the transitions.

Concentration Sample (PPM)	NDMA (in 50mg/ml API)			
	Concentration w.r.t. 50 mg/ml ranitidine	Accuracy (n=6) (Spiked Standard)	Precision (% RSD, n=6) (Spiked Standard)	Recovery (%) (n=6)
Control sample (50mg/ml ranitidine)	5 ng/ml	101.18%	3.19	(80-120)
LOD (0.01 ppm)	0.5 ng/ml	101.04%	1.49	(80-120)
LLOQ (0.03 ppm)	1.5 ng/ml	102.77%	2.5	(80-120)
Spec Level (0.09 ppm)	4.5 ng/ml	104.07%	1.43	(80-120)

Table 1. Details of concentrations analyzed using QTRAP 4500 system.

To learn more about this method please email: vendas@sciex.com

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