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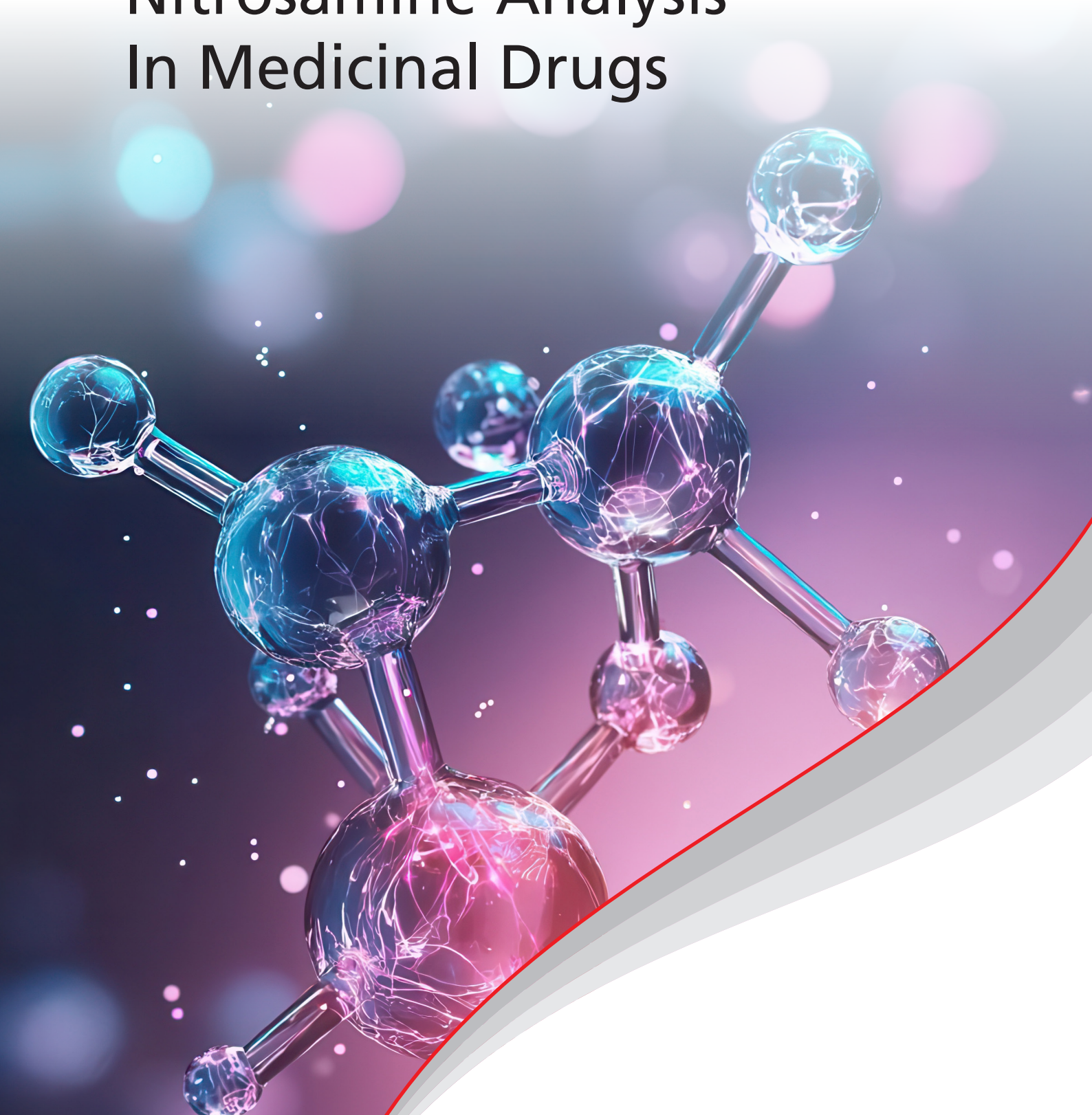
UFMS Approach For Nitrosamine Analysis In Medicinal Drugs

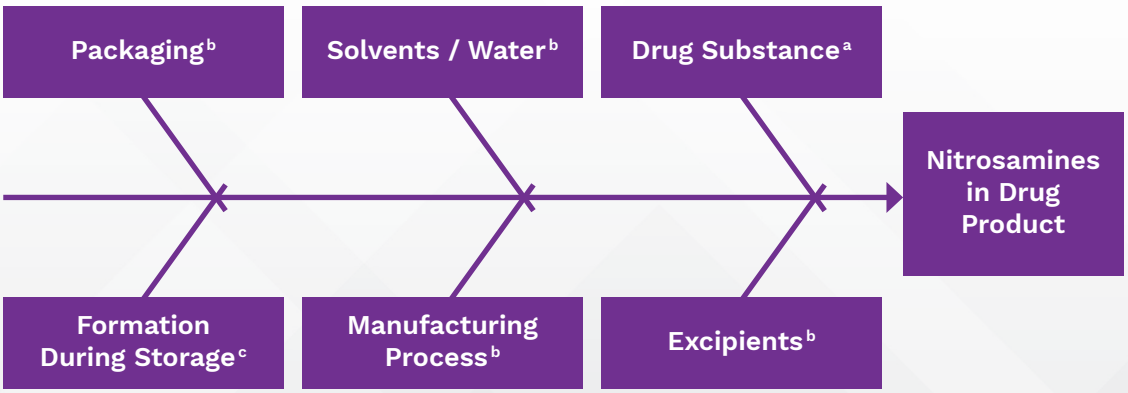


Introduction

Nitrosamines, also known as N-nitrosamines, refer to any molecule with a nitroso functional group (NO^+) bonded to a deprotonated amine. Nitrosamine impurities are of particular concern as there is evidence that they can be carcinogenic. Therefore, although they are present in some foods and drinking water supplies, their presence in medicines is considered unacceptable.

It is believed that nitrosamines are introduced into finished drug products as a result of the manufacturing process. Further investigations have proven that nitrosamines can also occur due to the active pharmaceutical ingredient's chemical structure or even the conditions in which they are stored or packaged (Figure 1).

Contents



[a]Primary / predominant source of potential nitrosamines
[b]Secondary sources of potential nitrosamines
[c]Formed by a mechanism other than degradation of the drug substance

Figure 1. Sources of nitrosamines in drug product (Reference: From USP PF Chapter 1469)

Presence of nitrosamines in medicinal drugs

In July 2018, the U.S. Food and Drug Administration (FDA) announced that the carcinogenic impurities NDMA and NDEA (Table 1) were detected in valsartan bulk drug substances, which are used to treat hypertension. Further investigations revealed the presence of other nitrosamines - such as NDIPA, NEIPA, NMBA, and NDBA - in various angiotensin II receptor blockers (ARBs), which resulted in many ARBs being recalled.

Shortly after, in September 2019, ranitidine – a prescription and over-the-counter drug used to treat acid reflux - was suspected of being contaminated with NDMA. Findings revealed that levels of NDMA in ranitidine may increase to unacceptable levels over time or when exposed to higher than room temperatures. Eventually, the FDA requested withdrawal of all remaining ranitidine products from the U.S. market.

In early 2020, the FDA began an investigation into the presence of NDMA in metformin, a prescription drug used to control high blood sugar in patients with type 2 diabetes. The investigation found above acceptable intake limits of NDMA in certain lots of extended-release (ER) metformin and recommended companies recall lots with levels of NDMA above the acceptable intake limit of 96 nanograms per day.

Additionally, the FDA have also investigated the presence of 1-methyl-4-nitrosopiperazine (MNP) in Rifampin and 1-cyclopentyl-4-nitrosopiperazine (CPNP) in rifapentine drug substance and drug products, which are antibacterial drugs used to treat tuberculosis.

The analysis of nitrosamine impurities at trace levels poses many challenges, including the solubility and thermal stability of nitrosamines and drug substances, and this type of investigation may require more than one analytical technique.

In this eBook, we explore the quantification of trace levels of nitrosamine impurities from various drug substances, drug products, and solvents. We also outline Shimadzu's UFMS series of LC-MS/MS and GC-MS/MS technologies, which promise high sensitivity powered by "Analytical Intelligence".

No.	Name	Abbr.	CAS No	Formula	MW
1	N-Nitrosodimethylamine	NDMA	62-75-9	C2H6N2O	74.1
2	N-Nitroso-N-methyl-4-aminobutyric acid	NMBA	61445-55-4	C5H10N2O3	146.2
3	N-Nitrosodiethylamine	NDEA	55-18-5	C4H10N2O	102.1
4	N-Nitrosoethylisopropylamine	NEIPA	16339-04-1	C5H12N2O	116.2
5	N-Nitrosodiisopropylamine	NDIPA	601-77-4	C6H14N2O	130.2
6	N-Nitrosodipropylamine	NDPA	621-64-7	C6H14N2O	130.2
7	N-nitrosomethylphenylamine	NMPA	614-00-6	C7H8N2O	136.2
8	N-Nitrosodibutylamine	NDBA	924-16-3	C8H18N2O	158.2

Table 1. List of commonly analyzed nitrosamines

Headspace GC-MS/MS Analysis of Nitrosamines in Losartan API As Per USP General Chapter Prospectus <1469> (Procedure 2)

Proposed United States Pharmacopeia (USP) General chapter <1469> aligns with current scientific and regulatory approaches to ensure the appropriate control of nitrosamine impurities in drug substances and drug products. The objective of this standard is to provide a science-based approach for the control of nitrosamine impurities, eliminating or reducing their presence in drug products.

This application data is based on procedure 2 of General Chapter Prospectus<1469>. Analysis details mentioned in said method were used with Shimadzu headspace autosampler and GCMS triple quadrupole system GCMS-TQ8050 NX with HS-20. In this application brief, we have analysed 3 more nitrosamines (NDPA, NDBA and NMPrZ) in addition to 4 mentioned nitrosamines (NDMA, NDEA, NEIPA and NDIPA) with eight times better sensitivity.

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System Description

System Configuration

GCMS System : GCMS-TQ8050 NX with HS-20
Column : SH-Stabilwax
(0.32 mm I.D. × 30 m, 1.0 µm)
Ionization Mode : Electron Ionization (EI)

Sample Information

NDMA, NDEA, NEIPA, NDIPA, NDPA, NDBA and NMPrZ in Losartan API

Reference Methods

Procedure 2 of USP General Chapter <1469 >

Benefits

- The GCMS-TQ8050 NX system easily meets the criteria as per the proposed USP general chapter <1469> procedure 2.
- The USP General Chapter is applicable to only 4 NSA's (NDMA, NDEA, NEIPA & NDIPA) whereas Shimadzu methodology can be used for quantitation of additional 3 NSA's. (NDPA, NDBA & NMPrZ)
- The Correlation coefficient (r^2) was greater than 0.999 for all the seven nitrosamines.

Representative Data

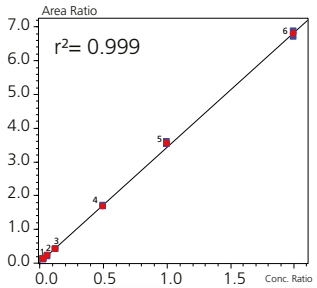

Figure 2: Calibration curve for NDMA

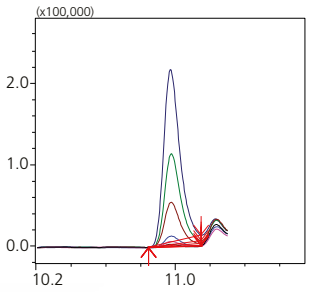

Figure 3: Overlay of linearity standards for NDMA

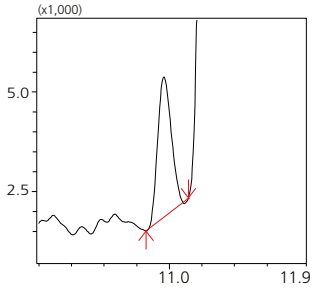

Figure 4: LOQ solution chromatogram for NDMA

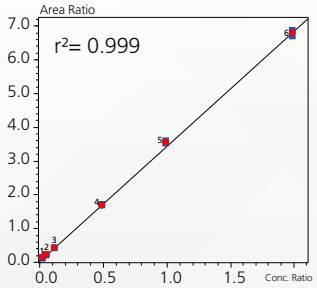

Figure 5: Calibration curve for NDEA

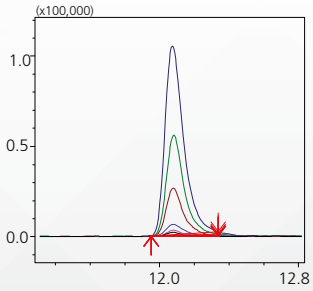

Figure 6: Overlay of linearity standards for NDEA

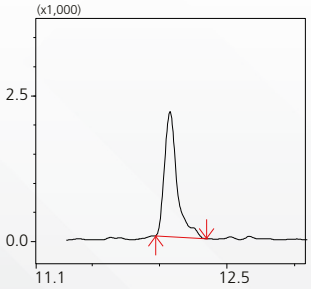

Figure 7: LOQ solution chromatogram for NDEA

Quantitation of 6 Nitrosamines in 5 Sartans By LC-MS/MS As Per Proposed USP General Chapter<1469> (Procedure 3)

5 different sartans namely olmesartan, telmisartan, irbesartan, losartan and valsartan were analyzed using methodology described in USP General Chapter Prospectus <1469> using Shimadzu LCMS-8045. Analysis was done for 6 recommended nitrosamines using internal standard (stable labelled isotopes) method of quantitation. Equivalent results were obtained using Raptor ARC-18 column.

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System Description

System Configuration

HPLC System : Nexera XS
Column : Raptor ARC-18 (3 mm I.D. × 150 mm, 2.7 µm)
LCMS System : LCMS-8045
Ionization Mode : APCI

Sample Information

NDMA, NMBA, NDEA, NEIPA, NDIPA and NDBA in Olmesartan, Telmisartan, Irbesartan, Losartan and Valsartan

Reference Methods

Procedure 3 of USP General Chapter <1469 >

Benefits

- The LCMS-8045 system easily meets the criteria as per the proposed USP general chapter <1469> procedure 3.
- Correlation coefficient was greater than 0.99 for all the six nitrosamines.

Representative Data

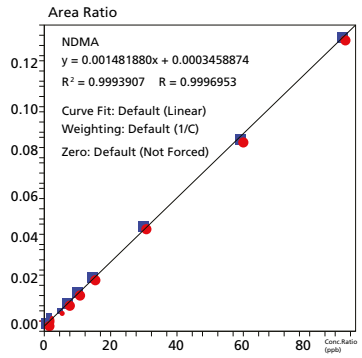


Figure 8: Calibration curve for NDMA

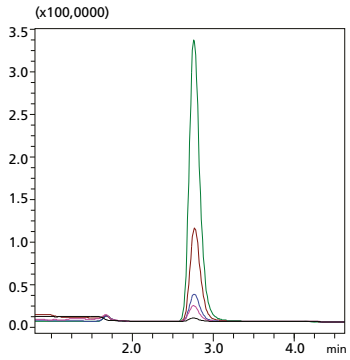


Figure 9: Overlay of linearity standards for NDMA

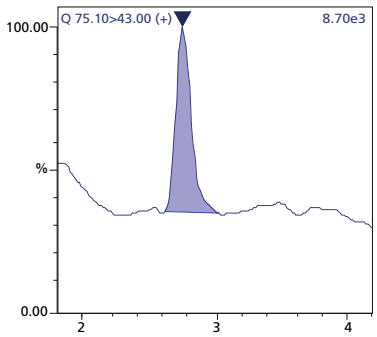


Figure 10: LOQ solution chromatogram for NDMA

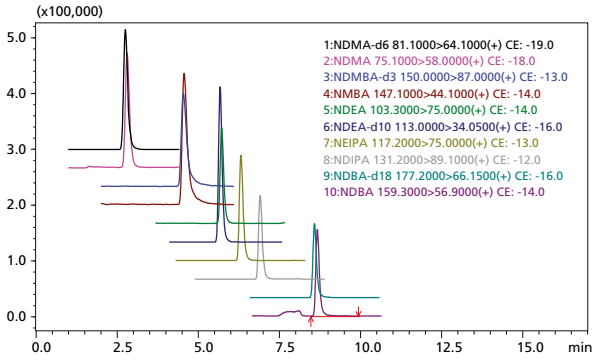


Figure 11: Representative LCMS chromatogram of 6 nitrosamines

High Sensitivity Analysis of 6 Nitrosamines in Olmesartan KSM Using LCMS-8060

Given application highlights applicability of LCMS-8060 for nitrosamine analysis at levels lower than recommended concentration. In this data we analyzed NDMA, NMBA, NDEA, NEIPA, NDIPA and NDBA impurities at lower concentrations in olmesartan KSM.

System Description

System Configuration

HPLC System : Nexera X2
Column : Shim-pack Arata C18
(3 mm I.D. × 150 mm, 2.2 µm)
LCMS System : LCMS-8060
Ionization Mode : APCI

Sample Information

NDMA, NMBA, NDEA, NEIPA, NDIPA and NDBA in Olmesartan KSM

Reference Methods

Procedure 3 of USP General Chapter <1469 >

Benefits

- Quantitation of NDMA,NMBA,NDEA,NEIPA, NDIPA and NDBA was performed on LCMS-8060 using APCI mode. Aqueous linearity was plotted from 0.1 ppb to 10 ppb for all six nitrosamines.
- Correlation coefficient was greater than 0.99 for all the six nitrosamines.

Representative Data

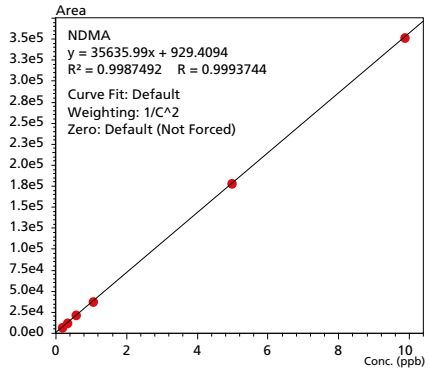


Figure 12: Calibration curve for NDMA

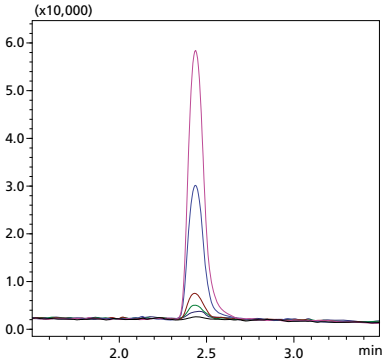


Figure 13: Overlay of linearity standards for NDMA (6 points)

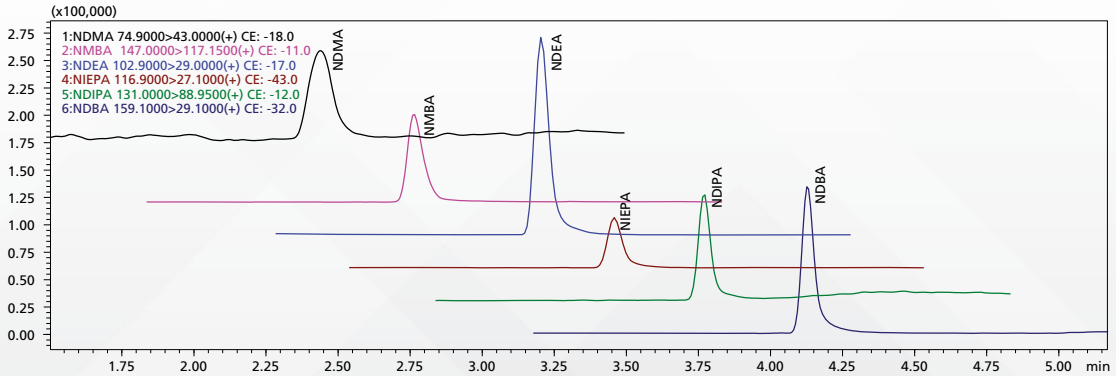


Figure 14: MRM chromatogram of 6 nitrosamines @ 5 ppb level

High Resolution Analysis of 7 Nitrosamines in Various Sartan Drug Substances Using LCMS-9030

Nitrosamine impurities are low molecular weight compounds and analyzed in trace concentrations. This situation directs us to sometimes consider use of high resolutions hybrid mass spectrometers like Quadrupole Time of Flight (QTOF) MS in order to confirm false positives.

In this application we share methodology for high resolution quantitation of 7 nitrosamine- NDMA, NMBA, NDEA, NEIPA, NDIPA, NDPA and NDBA in Losartan and Candesartan drug substances.

System Description

System Configuration

Column : Shim-pack Solar C18 (4.6 mm I.D. × 250 mm, 5 µm)
LCMS System : LCMS-9030 (Q-TOF)
Ionization Mode : DUIS*
*Simultaneous ESI/APCI

Sample Information

NDMA, NMBA, NDEA, NEIPA, NDIPA, NDPA and NDBA in Losartan and Candesartan

Reference Methods

FDA method dated on 21 May 2019, LC-HRMS Method for the Determination of Six Nitrosamines in ARB Drugs

Benefits

- Refer to the FDA reference method, a targeted MS/MS HRMS method was used in data acquisition and 15 ppm mass accuracy tolerance was applied in data analysis.

Representative Data

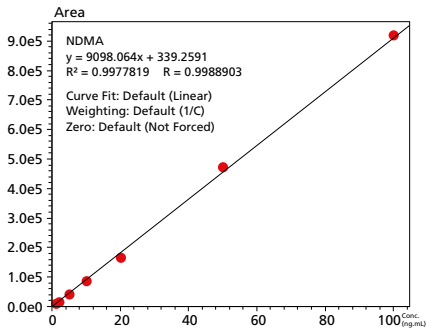


Figure 15: Calibration curve for NDMA

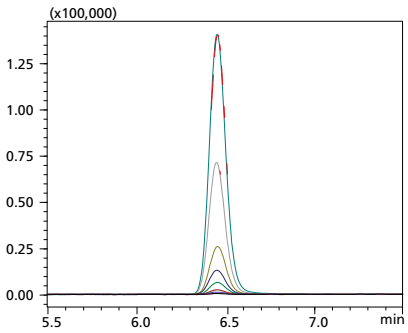


Figure 16: Overlay of linearity standards for NDMA (9 points)

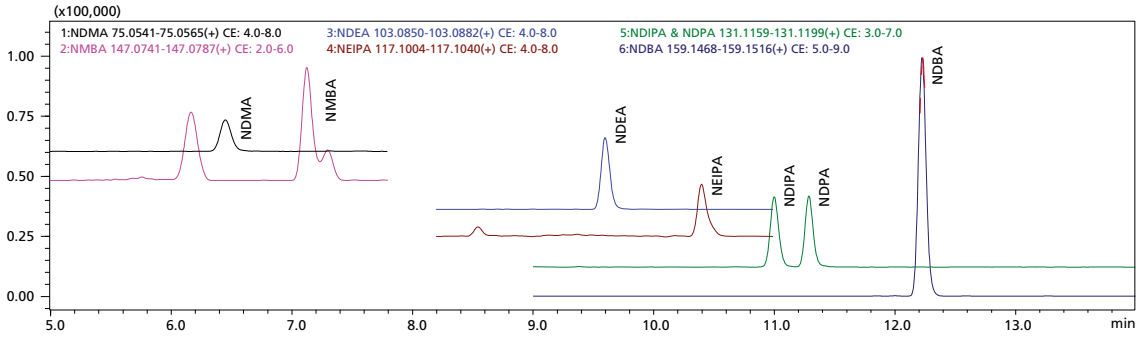


Figure 17: MRM chromatogram of 7 nitrosamines (10.0 ppb; NDBA 5.0 ppb)

Quantitation of 8 Nitrosamines in Metformin ER (Extended Release) Tablets and Placebo Using LCMS-8045

In this experiment, we analyzed 8 nitrosamines—NDMA, NMBA, NDEA, NEIPA, NDIPA, NDPA, NDBA and NMPA in metformin ER tablets and placebo using in-house developed method with liquid-liquid extraction being employed for sample preparation.

All 8 nitrosamines were quantified with the specification level of 0.01 ppm with respect to the sample concentration at 200 mg/mL. Analyzed metformin ER tablet and placebo were found to be negative for any nitrosamine impurities.

System Description

System Configuration

HPLC System : Nexera series
Column : Shim-pack Scepter (4.6 mm I.D. × 250 mm, 5.0 µm)
LCMS System : LCMS-8045
Ionization Mode : APCI

Sample Information

NDMA, NMBA, NDEA, NEIPA, NDIPA, NDPA, NDBA and NMPA in Metformin ER

Reference Methods

FDA method dated on 3 June 2020, LC-ESI-HRMS Method for the Determination of Nitrosamine Impurities in Metformin Drug Substance and Drug Product

Benefits

- LCMS-Quantification method for eight nitrosoamines has been successfully developed in LCMS-8045 with Nexera series.
- All the eight nitrosoamines were quantified with the specification limit of 0.01 ppm.
- Aqueous linearity was plotted from 0.5 ppb to 25 ppb for all eight nitrosamines. Correlation coefficient was greater than 0.99 for all the eight nitrosamines.

Representative Data

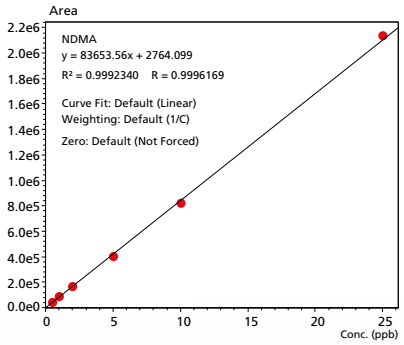


Figure 18: Calibration curve for NDMA

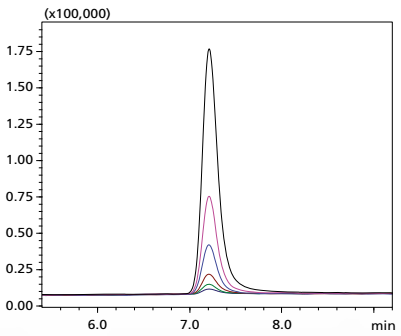


Figure 19: Overlay of linearity standards for NDMA (6 points)

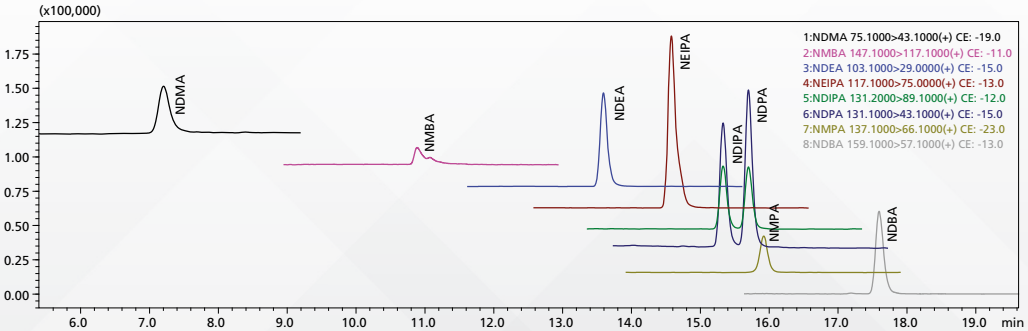


Figure 20: MRM chromatogram of 8 nitrosamines (5.0 ppb)

Quantification of N-nitroso-dimethylamine (NDMA) in Metformin Tablets Using LCMS-8045

Sometimes quantitation of NDMA is hampered due to close elution of DMF. In this study, we developed a method using Shimadzu Shim-pack phenyl column and gradient program to chromatographically separate DMF from NDMA.

System Description

System Configuration

HPLC System : Nexera series
Column : Shim-pack Phenyl
(4.6 mm I.D. × 150 mm, 5.0 µm)
LCMS System : LCMS-8045
Ionization Mode : APCI

Sample Information

NDMA in Metformin Tablets

Reference Methods

FDA method dated on 4 February 2020, LC-HRMS Method for the Determination of NDMA in Metformin Drug Substance and Drug Product

Benefits

- LCMS-Quantification method for NDMA has been successfully developed in LCMS-8045 with Nexera series.
- NDMA was quantified with the specification limit of 0.03 ppm.
- DMF has been well separated from NDMA peak, hence no interference observed due to DMF.

Representative Data

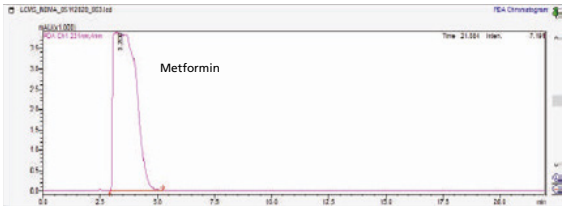


Figure 21: Metformin peak observed at about 3.2 RT at 231nm

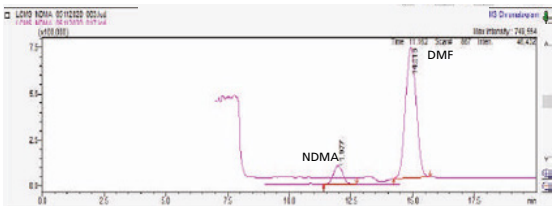


Figure 22: DMF has been well separated from NDMA peak, hence no interference is observed

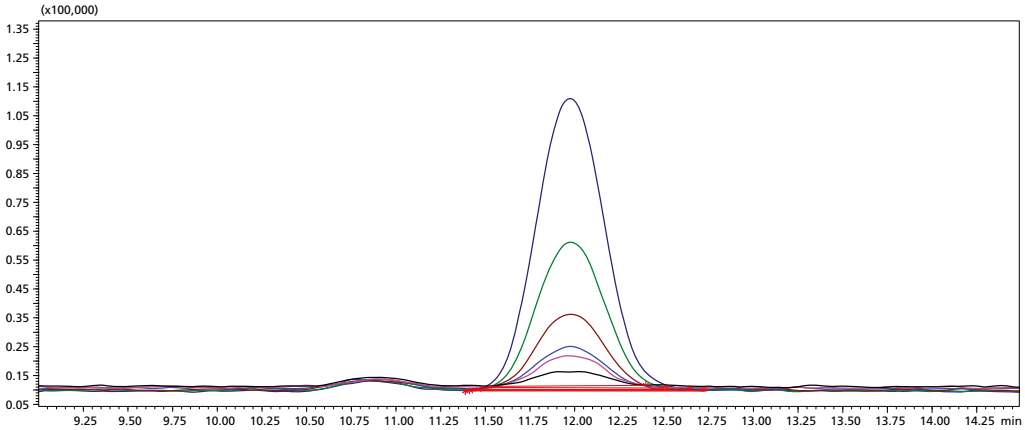


Figure 23: Overlay of NDMA linearity levels

LC-HRMS Method For Analysis of 8 Nitrosamines in Metformin Drug Substance Using LCMS-9030

In this application, we showcase high resolution quantitative analysis of 8 nitrosamines— NDMA, NMBA, NDEA, NEIPA, NDIPA, NDPA, NDBA and NMPA in metformin hydrochloride. Analysed sample was found to be negative for 8 tested nitrosamines.

Click here

System Description

System Configuration

Column : Shim-pack Solar, C18 (4.6 mm I.D. × 250 mm, 5 µm)
LCMS System : LCMS-9030 (Q-TOF)
Ionization Mode : DUIS*
*Simultaneous ESI/APCI

Sample Information

NDMA, NMBA, NDEA, NEIPA, NDIPA, NDPA, NDBA and NMPA in Metformin, Losartan and Candesartan

Reference Methods

FDA method dated on 3 June 2020, LC-ESI-HRMS Method for the Determination of Nitrosamine Impurities in Metformin Drug Substance and Drug Product

Benefits

- Simultaneous analysis of up to eight N-nitrosamine impurities in drug substances by LC-HRMS method on LCMS-9030.
- A targeted MS/MS (TOF) method with 2 *m/z* isolation window by the quadrupole was optimized to obtain best sensitivity.
- A mass tolerance of (±)15 ppm was adopted to produce extracted-ion chromatograms (XICs) for quantitation.

Representative Data

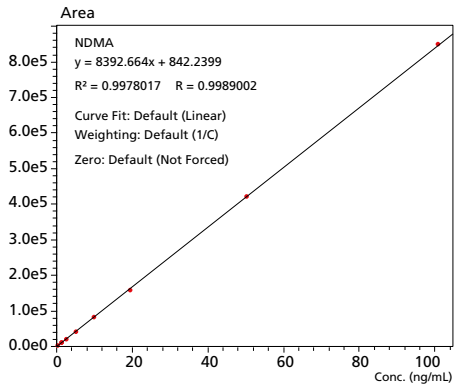


Figure 24: Calibration curve for NDMA

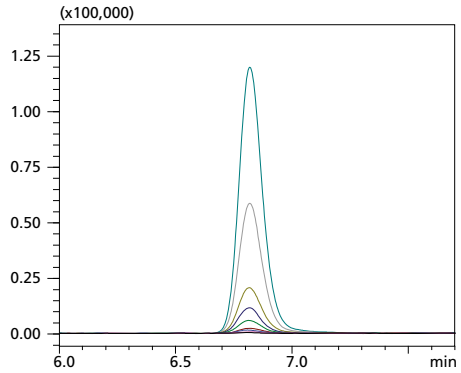


Figure 25: Overlay of linearity standards for NDMA (6 points)

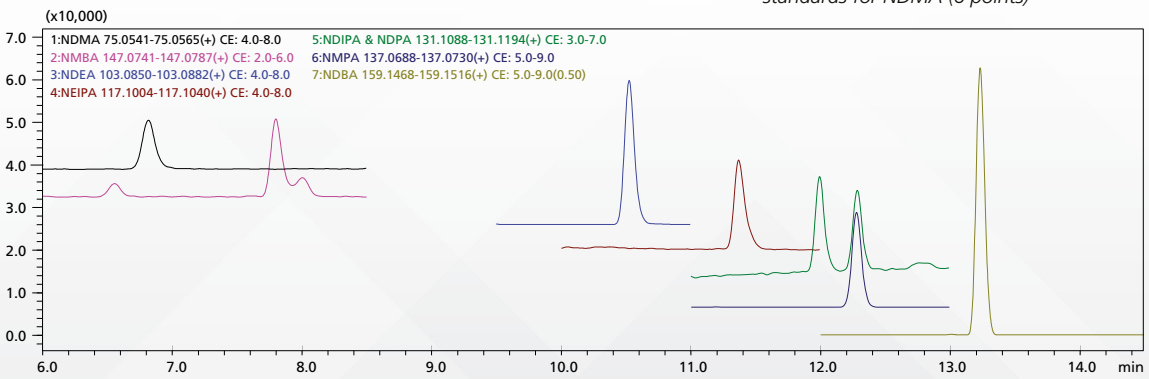


Figure 26: MRM chromatogram of 8 nitrosamines (5.0 ppb)

Quantitative Analysis of NDMA in Ranitidine Drug Substance Using LCMS-8045

Levels of NDMA in ranitidine may increase to unacceptable levels over time and when exposed to higher than room temperatures. Based on these findings, ranitidine is withdrawn from US markets.

In this application we analyze trace levels of NDMA in ranitidine drug substance using LCMS-8045 using methodology described by US FDA.

System Description

System Configuration

HPLC System : Nexera X2
Column : ACE Excel C18-AR
(4.6 mm I.D. × 50 mm, 3 µm)
LCMS System : LCMS-8045
Ionization Mode : APCI

Sample Information

NDMA in Ranitidine

Reference Methods

FDA method dated on 17 October 2019, LC-MS/MS Method for the Determination of NDMA in Ranitidine Drug Substance and Solid Dosage Drug Product

Benefits

- The USFDA LC-MS/MS Quantification method for NDMA in Ranitidine has been successfully applied in LCMS-8045.
- NDMA was quantified with the LOQ level of 0.033 ppm with respect to the sample concentration at 30 mg/mL.
- Linearity was plotted from 1 ppb to 100 ppb for NDMA. Correlation coefficient was greater than 0.999.

Representative Data

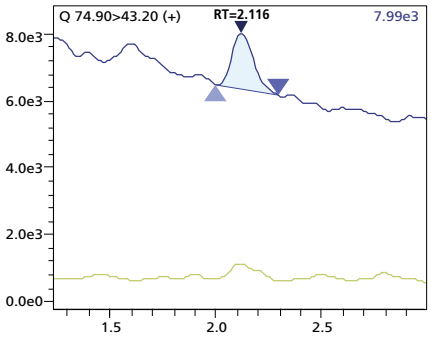


Figure 27: MRM chromatogram NDMA at LOQ level

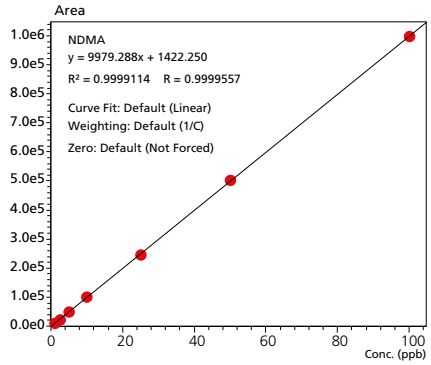


Figure 28:Calibration curve for NDMA

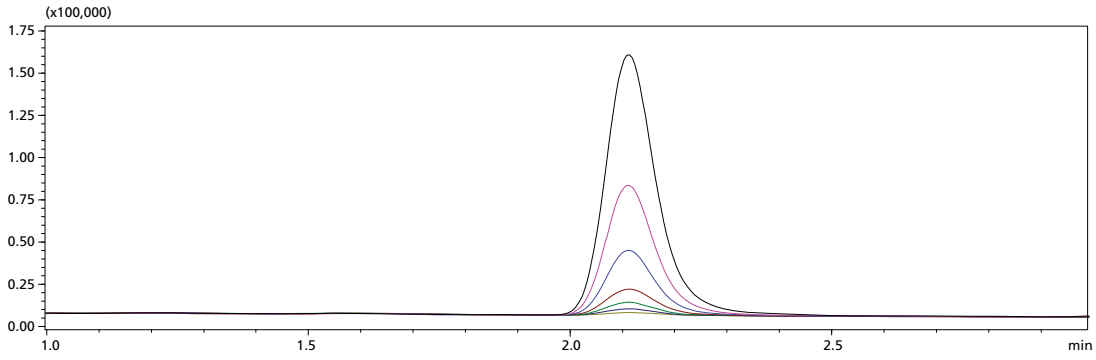


Figure 29: Overlay of linearity standards for NDMA (7 points)

Quantitative Analysis of NMBA in Tenofovir Disoproxil Fumarate Using LCMS-8060

This application deals with high sensitivity analysis of NMBA in tenofovir drug substance.

System Description

System Configuration

HPLC System : Nexera X2
Column : Shim-pack GISS C18
(4.6 mm I.D. × 250 mm, 5 µm)
LCMS System : LCMS-8060
Ionization Mode : APCI

Sample Information

NMBA in Tenofovir disoproxil fumarate

Benefits

- NMBA was quantified with the LOQ level of 0.002 ppm with respect to the sample concentration at 50 mg/mL.
- Linearity was performed over a range of 0.05 ng/ mL to 50.00 ng/mL with the coefficient of correlation of 0.999.

Representative Data

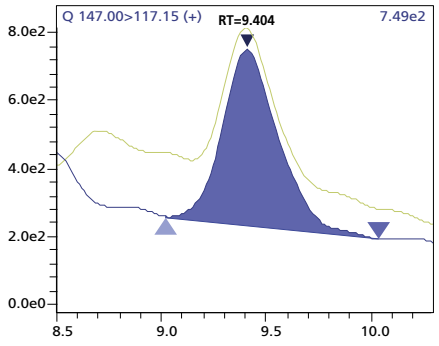


Figure 30: MRM chromatogram NMBA at LOQ level

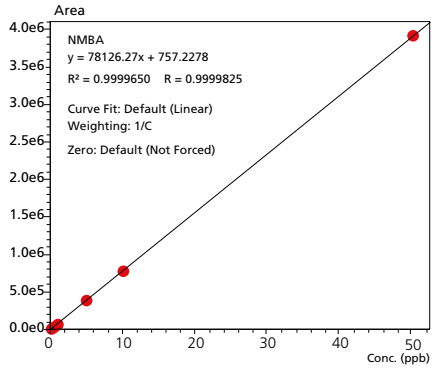


Figure 31: Calibration curve for NMBA

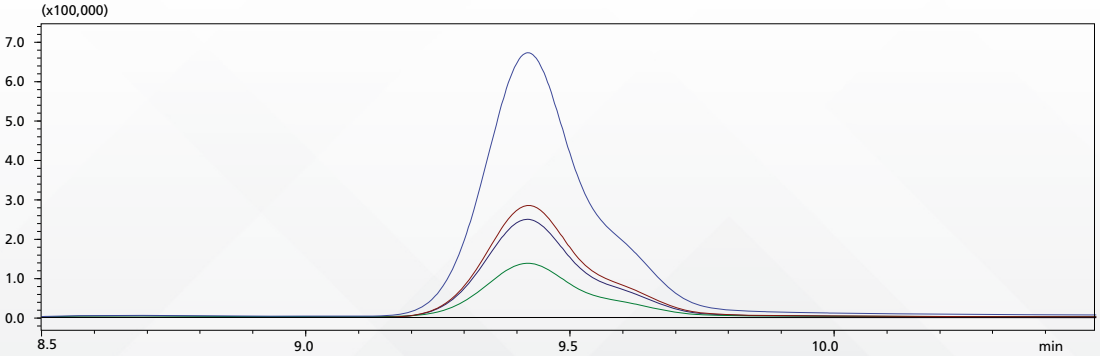


Figure 32: Overlay of linearity standards for NMBA (7 points)

Quantitative Analysis of Nitrosamines in 5 Different Solvents Using GCMS-TQ8040 NX

Recovered materials such as solvents, reagents, and catalysts pose a risk of nitrosamine impurities due to the presence of residual amines (such as trimethylamine or diisopropylethylamine). Quenching step (i.e., nitrous acid used to decompose residual azide) can be a potential source for introduction of nitrosamines during solvent recovery process.

In this application we analysed NDMA, NDEA, NEIPA, NDIPA and NDBA in DMF (HS grade), IPA, DMF, DMF-IPA and DMF-Water. Solvent samples were either injected as such or diluted to 10,000 times in DCM. These samples were analysed using Shimadzu GCMS-TQ8040 NX with AOC-20i Plus autosampler.

System Description

System Configuration

GCMS System : GCMS-TQ8040 NX with AOC-20i Plus
Column : VF Wax MS (0.25 mm I.D. × 30 m, 1.0 µm)
Ionization Mode : Electron Ionization (EI)

Sample Information

NDMA, NDEA, NEIPA, NDIPA, NDPA and NDBA in DMF, IPA, DMF, DMF-IPA and DMF-Water

Benefits

- Linearity was performed over a range of 1.0 ppb to 16.0 ppb for NDMA, NDEA, NEIPA, NDIPA and 2.0 ppb to 32 ppb for NDBA.
- The Correlation coefficient (r^2) was greater than 0.99 for all the six nitrosamines.

Representative Data

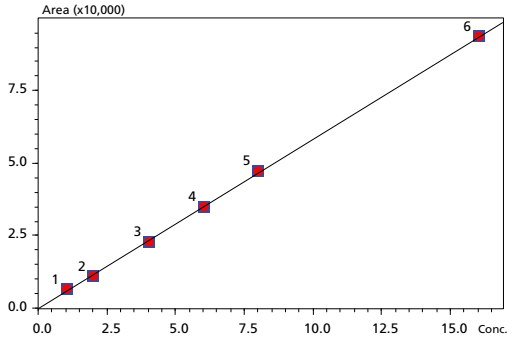


Figure 33: Calibration curve for NDMA

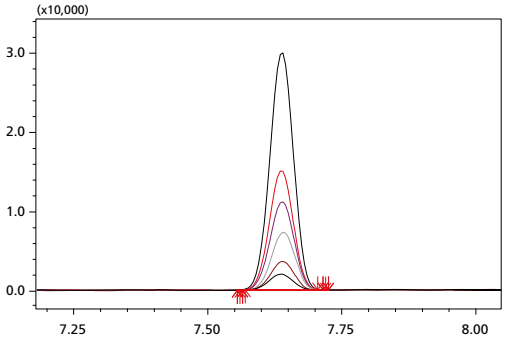


Figure 34: Chromatographic overlay of linearity levels of NDMA

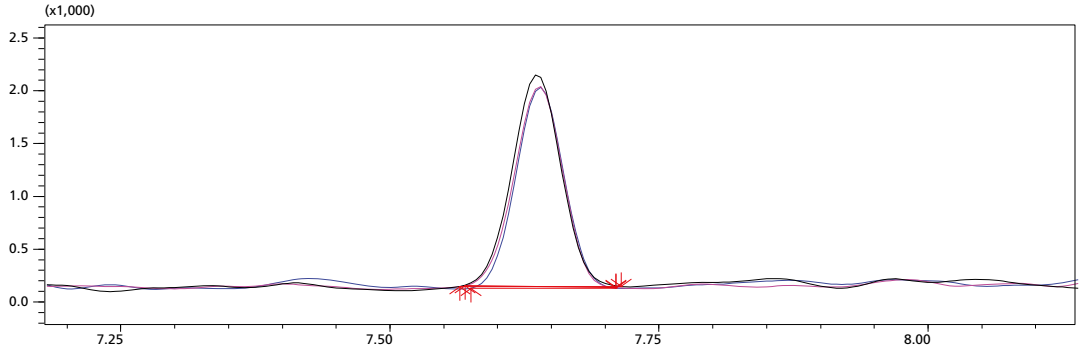


Figure 35: Top chromatographic overlay of LOQ (n=3, NDMA)

Quantitative Analysis of 8 Nitrosamine Impurities in 12 Different Solvents Using LCMS-8045

8 nitrosamines, namely NDMA, NMBA, NDEA, NEIPA, NDPA, NDIPA, NMPA and NDBA were analysed in different solvent systems using internal standard (stable labelled isotopes) method of quantitation.

Samples were prepared based on the solvent properties and three different sample pretreatment methods were employed-direct method, evaporator method and dilution method.

Click here

System Description

System Configuration

HPLC System : Nexera XS
Column : Shim-pack GIST C18-AQ (4.6 mm I.D. × 100 mm, 3 µm)
LCMS System : LCMS-8045
Ionization Mode : APCI

Sample Information

NDMA, NMBA, NDEA, NEIPA, NDIPA, NDPA, NMPA and NDBA in 12 Different Solvents

Benefits

- A single LC-MS/MS method for the determination of 8 nitrosamines in 12 solvents.
- It easily meets the current regulatory requirement i.e. 0.03 ppm for the nitrosamines
- The same method can be extended for the other solvents

Table 2: Tabulation of boiling points and method of sample preparation

No.	Solvents	Boiling Points (°C)
1	Dichloromethane(DCM)	40
2	Acetone	56
3	Chloroform	61
4	Methanol	65
5	Ethyl Acetate	77
6	Ethanol	78
7	Acetonitrile	82
8	Isopropanol	82
9	Water	100
10	Toluene	111
11	Dimethyl Formamide (DMF)	153
12	Dimethyl Sulfoxide (DMSO)	189

Evaporation Direct injection Dilution

Representative Data

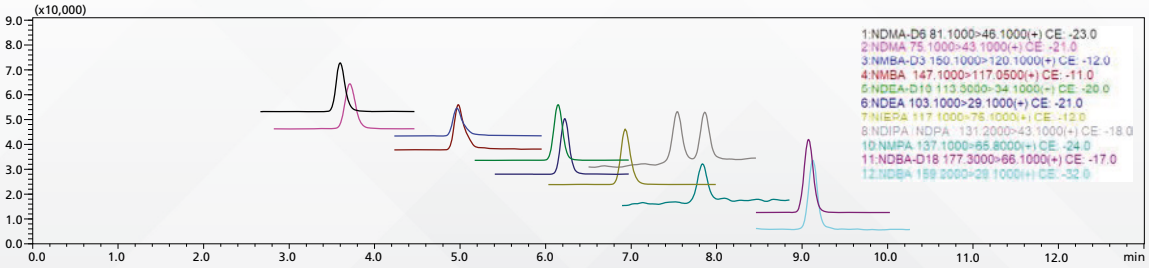


Figure 36: Representative MRM chromatogram

GCMS-TQ8050 NX with HS-20 NX

Shimadzu's Ultra High Sensitivity Triple Quadrupole GC-MS with Headspace autosampler for Pharma Impurity Analysis

Click here

Equipped with a new, highly efficient detector and three forms of noise reduction technologies, the GCMS-TQ8050 NX is capable of performing unprecedented quantitative analyses of ultra-trace amounts, down to femtogram level. Moreover, with its ultra-high sensitivity and high mass resolution, a whole new realm of quantitative analysis is offered, with reduced long –term operational costs and greater uptimes along with HS-20 NX headspace autosampler.

UFMS Throughput

UFMS ensures no compromise in sensitivity even when you run applications at maximum speed. This allows you to perform both Targeted screening and Quantitation with the same confidence. The combination of multiple injection modes (liquid or headspace) and acquisition modes (MRM, SIM or Scan) are designed to cater to all your impurity analysis needs. This can be performed with maximum ease and flexibility.

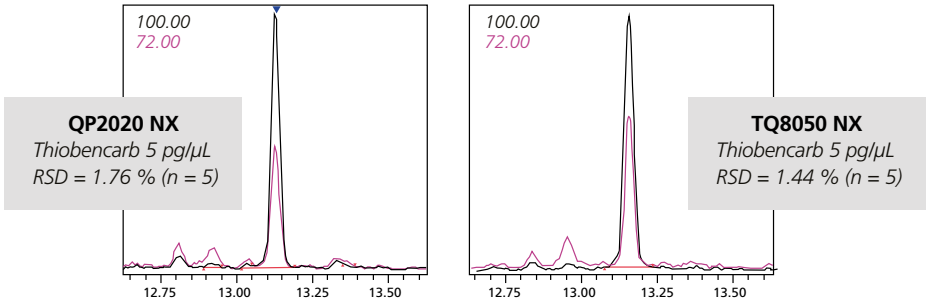


Figure 37: MSMS – two instruments in one. Use GC-MS and GC-MS/MS functions interchangeably with no compromise in sensitivity and selectivity

Minimal Carryover

In high throughput labs, where time is money, you don't want to spend time doing trouble-shooting and reanalysis. One of the key contributors to this trouble is the transfer line between headspace and GCMS. Shimadzu HS-20 NX is equipped with not only the shortest but also most inert transfer line. In the residual solvents analysis of medicines, analysis with an aqueous solvent may be performed after analysis with a DMF solvent, but with the HS-20 NX, carryover of DMF is not a problem. HS-20 NX is effective for the analysis of samples with different type of solvents or large concentration differences.

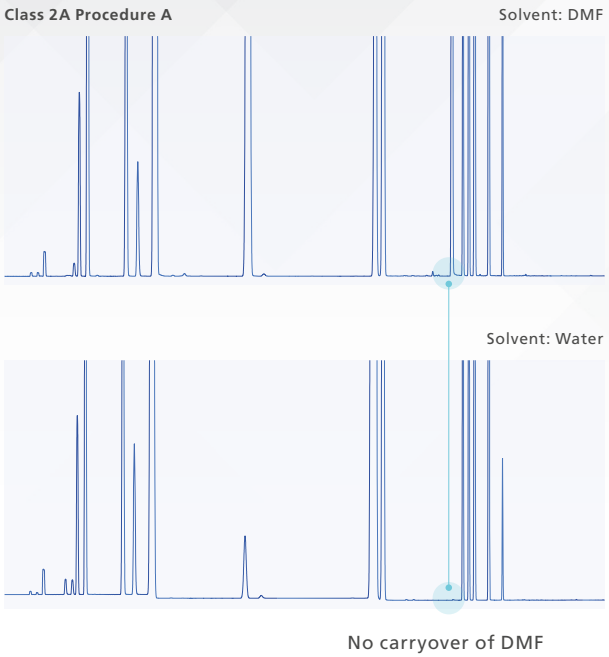
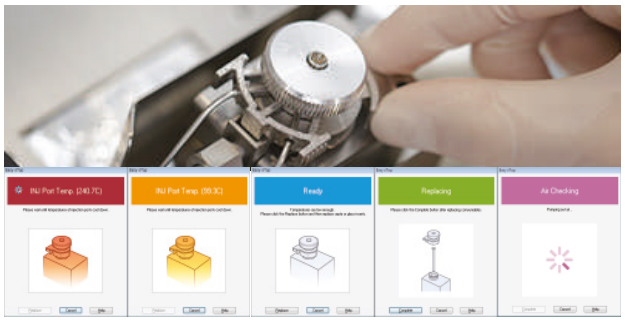


Figure 38: Residual solvents analysis in pharmaceuticals USP <467> Class 2A

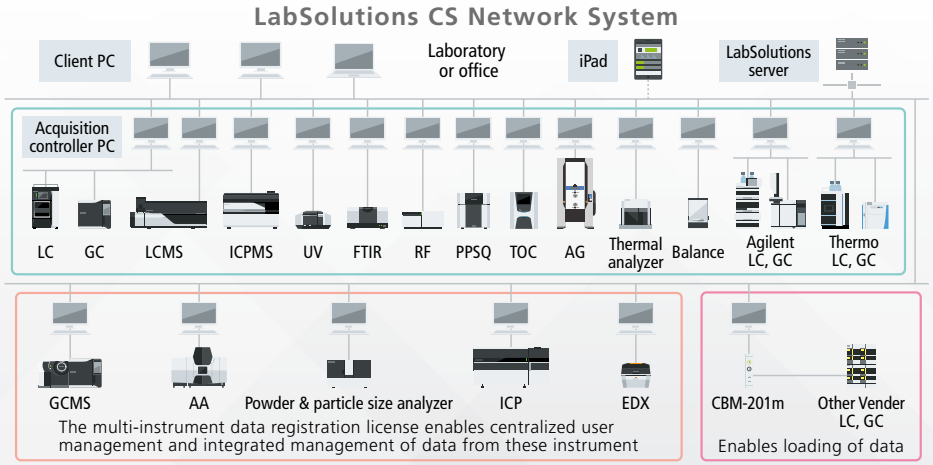
Minimal Maintenance

In rush of work, we need our instruments to make life easy for us. Regular tasks like maintaining the injection port or installing column are made super easy and hassle free using ClickTek and Easy sTop function. Active Time Management helps plan work schedules by giving clear estimates of autotuning, batch completion, time management during maintenance etc.



Regulatory Compliance

Rest assured that data integrity and authenticity is maintained in accordance with industry regulation norms such as FDA 21 CFR Part 11. Your data is always backed up and protected from unauthorised access. We continuously provide enhanced solutions and upgrades to keep up with regulators direction.



LCMS-8045/ LCMS-8060NX

Powered by Analytical Intelligence, LCMS-80XX series LC-MS/MS are sensitiveand rugged solutions for impurity analysis-For both R&D and Pharma QC

Click here

UFMS capability of LCMS-8045 and LCMS-8060NX series ensures you don't miss any peaks, however closely eluting! Choose LCMS-8045 as a daily work horse in your QC labs with complete compliance in combination with LabSolutions CS, and LCMS-8060NX for increasing sensitivity, throughput with low injection volume and robustness. What's more - You can always upgrade LCMS-8045 to LCMS-8060NX.

UFscanning & UF-MRM with High Sensitivity

Equipped with a heated ESI probe, the LCMS-8060NX has the highest sensitivity in its class. It is capable of providing accurate and stable data over long periods of time. The inclusion of Shimadzu's ultra-high-speed high-voltage power supply enables the world's fastest scan speed (30,000 u/s) and polarity switching time (5 ms). High-speed acquisition benefits the laboratory by reducing run times for increased throughput, and also shortens method development time.

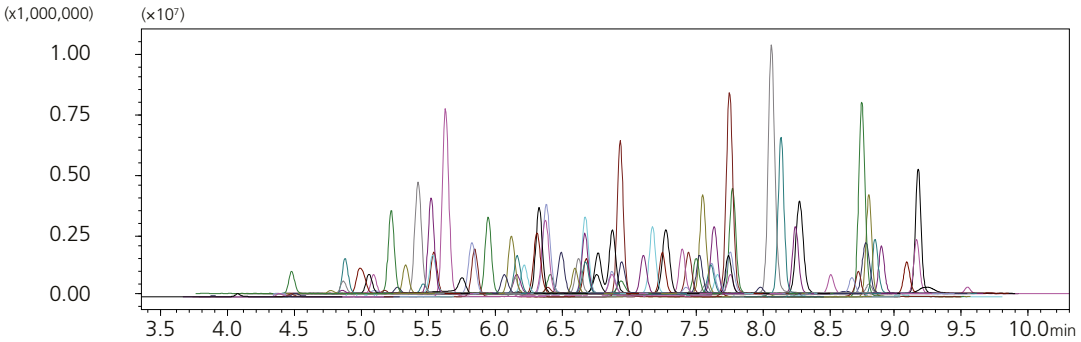


Figure 39: MRM chromatogram of 100 pesticides (0.02 ppm) in crops

Superior Robustness

The LCMS-8045 is designed to be robust. The heated ESI probe, high-temperature heating block, heated desolvation line, drying gas, and focusing optics all act to maximize sensitivity and minimize contamination. This means long periods of continuous operation in the laboratory with reliable data collection. Building up on these features, LCMS-8060NX boasts of 6 times more sensitivity and unsurpassed robustness owing to newly designed IonFocus unit and re-engineered ion guide system.

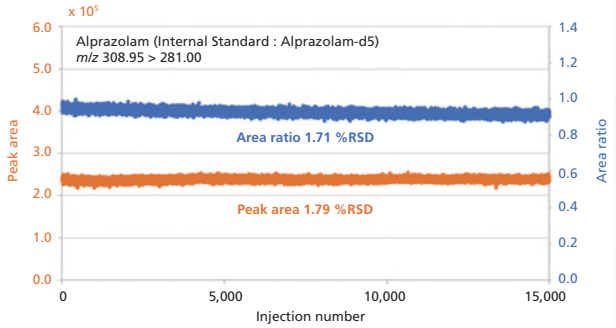
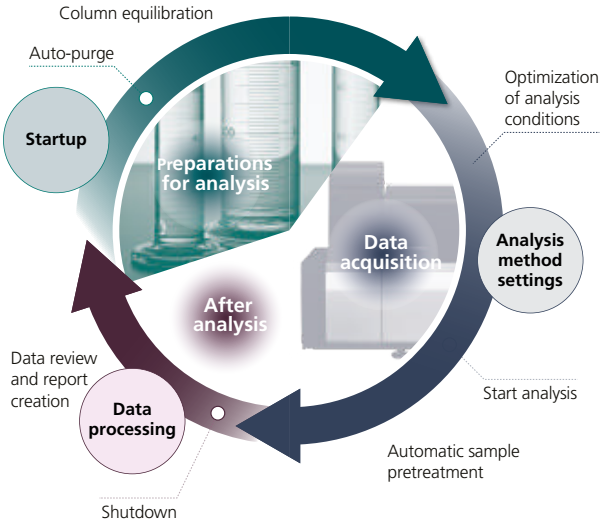


Figure 40: Results from consecutive analyses of Alprazolam-spiked human blood plasma by LCMS-8060NX

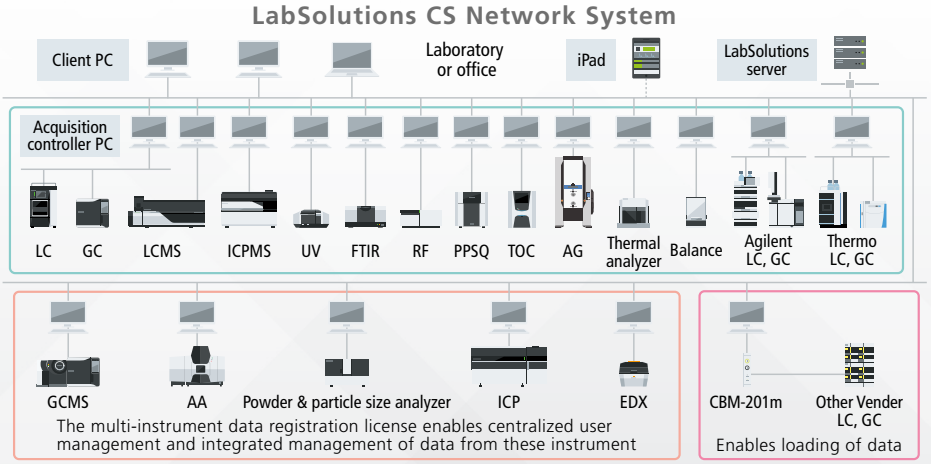
Easy Workflow

LabSolutions LCMS features an intuitive user interface. It offers the latest features designed to enhance laboratory productivity and streamline workflows with complete compliance. Analytical Intelligence of LCMS-8060NX with the Nexera UHPLC improves the efficiency of your entire workflow and maximizes laboratory throughput.



Regulatory Compliance

Simple and easy to use workflows are inherently designed to deliver compliance. Your data is always backed up and protected from unauthorized access. We continuously provide enhanced solutions and upgrades and keep up with regulators direction.



LCMS-9030

The LCMS-9030 quadrupole time-of-flight (QTOF) mass spectrometer integrates the world's fastest and most sensitive quadrupole technology with TOF architecture- making it a perfect solution for both qualitative assessment and quantitative determination of pharmaceutical impurity

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A product of Shimadzu's engineering DNA, speed and effortless performance enable the LCMS-9030 to address qualitative and quantitative challenges with genuine confidence and ease. The LCMS-9030 uses newly patented technologies to deliver both high resolution and accurate mass-attributes essential for confident formula assignment and unknown identification.

Excellence in Mass Measurement Accuracy (MMA)

Mass measurement accuracy (MMA) is the key performance attribute underlying all application fields using high-resolution accurate-mass (HRAM) spectrometers. The LCMS-9030 delivers the MMA needed for high-confidence identification of unknown compounds with an unprecedented level of stability. New technologies implemented in the Intelligent Temperature Control System and the UF-FlightTube makes it possible to accurately offset the changes occurring to both internal and external environments.

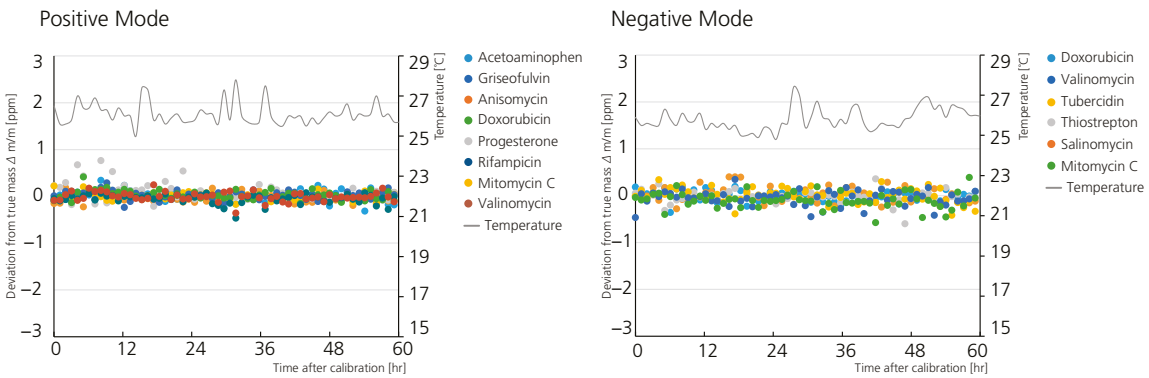

Figure 41: Graphical representation of measured accurate masses of all compounds

High MMA Over Wide Concentrations

The LCMS-9030 breaks new ground for quantitative analysis not only by its high sensitivity but also by the selectivity afforded by high MMA over a wide range of concentrations. Genuine ion statistics ensure that all measurements throughout the peak elution result within a narrow *m/z* window of the extracted ion chromatogram (XIC). Moreover, stability of MMA allows the same XIC setting to be comfortably used for series of analyses.

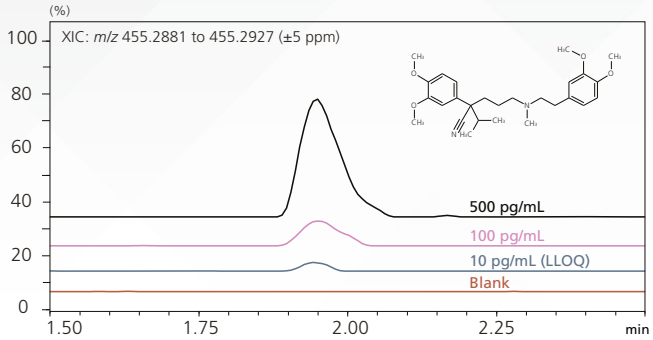

Figure 42: XIC of Verapamil [M + H]+ (exact mass 455.29042)

Same MMA Across Acquisition Modes

MS/MS spectra are a key tool for structural elucidation of unknown compounds, and ease of data interpretation is directly dictated by the MMA of MS/MS acquisition. This makes the LCMS-9030 an ideal instrument for structural analysis as its MS/MS mode achieves equally high MMA as the MS mode, thanks to the collision cell technologies that generate high-abundance fragment ions.

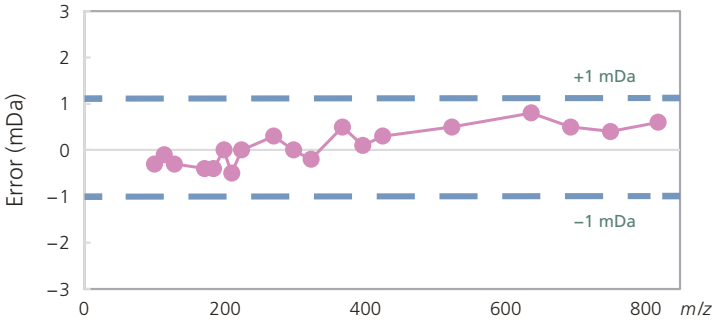

Figure 43: Mass error of product ions

HRAM for Selective Detection of Isobaric Compounds

The LCMS-9030 produces the high-resolution accurate mass data needed to distinguish between compounds having the same nominal mass. Even with incomplete chromatographic separation isobaric compounds can be detected as an isolated ion without cross talk.

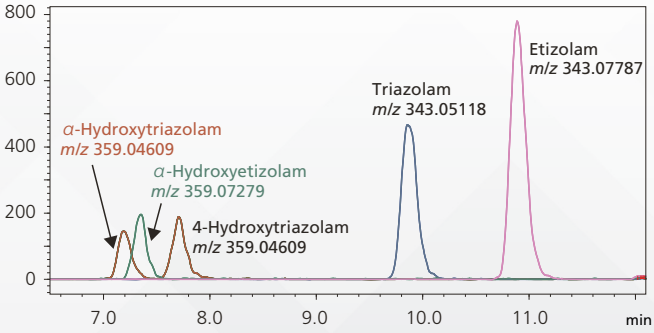

Figure 44: LCMS-9030 mass chromatogram of Etizolam, Triazolam, and metabolites spiked at 10 ng/mL in whole blood.

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GCMS-TQ8050 NX
by Shimadzu Corporation

Ease of use: ★★★★★
After-sales service: ★★★★★
Value for money: ★★★★★

Rating: ★★★★★

"We can't reach any conclusion without this analysis"

Kishor Bhalerao,
Garware Polyester Ltd.

LCMS-8060NX
by Shimadzu Corporation

Ease of use: ★★★★★
After-sales service: ★★★★½
Value for money: ★★★★★

Rating: ★★★★½

"Very useful instrument for ultrasensitive analysis."

Yuri Dzhurko,
Quinta-Analytica, Yaroslavl.

LCMS-9030
by Shimadzu Corporation

Ease of use: ★★★★★
After-sales service: ★★★★½
Value for money: ★★★★★

Rating: ★★★★★

"We use it on a daily basis and would not replace it with another machine."

Milen Kadiyski,
Aurubis, Bulgaria.

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