Nitrosamines: Overview & Solutions

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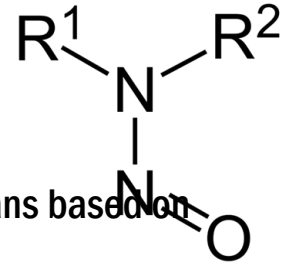
22 March 2024

phenomenex

Nitrosamine Impurities in Drugs



- Nitrosamines, or N-nitrosamines, are chemical compounds believed to be carcinogenic to humans based on animal studies.
- Therefore, nitrosamines need to be highly regulated to ensure that there is no adverse effect to human health.
- In 2018, multiple nitrosamines including NDMA were detected within various blood pressure medicines known as ‘sartans’.
- Since then, nitrosamines have been detected in ranitidine, metformin, and several other drugs which highlighted that the issue was not solely limited to sartans.
- The issue has resulted in multiple product recalls worldwide, with the problem likely to continue for some time as more drug products become implicated.
- Regulatory agencies (FDA, EMA, USP, Health Canada, etc.) were quick to act in establishing guidance for nitrosamine limits, testing, and risk assessment for prevention of nitrosamine formation in drug substance (API) and drug products.

Nitrosamine Formation in Drugs

Figure 1. Representative Reaction to Form Nitrosamines

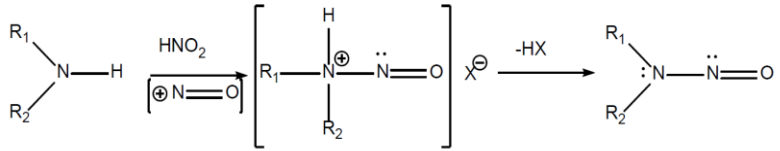
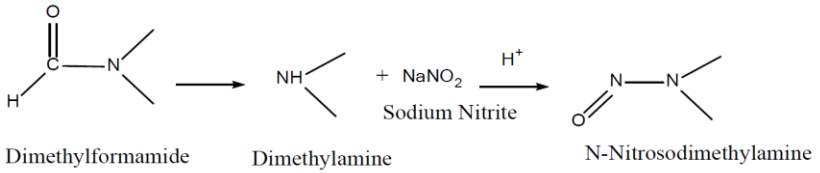


Figure 3. Formation of NDMA From N,N-Dimethylformamide



- Formation of nitrosamines is possible in the presence of secondary, tertiary, or quaternary amines and nitrite salts under acidic reaction conditions. Under these conditions, nitrite salts may form nitrous acid, which can react with an amine to form a nitrosamine (see Figure 1).
- Amide solvents, which are susceptible to degradation under certain reaction conditions, are another source of secondary amines. For example, under high reaction temperatures for an extended reaction period, N,N-dimethylformamide can degrade into dimethylamine, which can react with nitrous acid to form NDMA (see Figure 3).

Source: FDA - Control of Nitrosamine Impurities in Human Drugs: Guidance for Industry, 2021

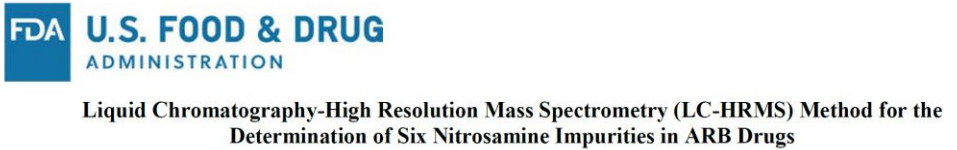
USP General Chapter <1469>

- 7 Nitrosamine Reference Standards available
- 4 Analytical Procedures
  - Quantitation of NDMA, NDEA, NDIPA, NEIPA, NMBA, NMPA, and NDBA in selected sartans (valsartan, irbesartan, and losartan potassium) by HPLC–HRMS on **Kinetex F5 (L43)** 2.6 µm 100 x 4.6 mm.
  - Quantitation of NDMA, NDEA, NDIPA, and NEIPA in selected sartans (valsartan, irbesartan, losartan potassium, olmesartan medoxomil, candesartan cilexetil, and telmisartan) by headspace GC–MS on **Stabilwax (G16)** 30 m x 0.32 mm x 1.0 µm.
  - Quantitation of NDMA, NDEA, NDIPA, NEIPA, NMBA, and NDBA in selected sartans (valsartan, losartan potassium, olmesartan medoxomil, candesartan cilexetil, and telmisartan) by HPLC–MS/MS on **Raptor ARC-18 (L1)** 2.7 µm 150 x 3.0 mm.
  - Quantitation of NDMA, NDEA, NDIPA, NEIPA, NMPA, and NDBA in selected sartans (valsartan, losartan potassium, and candesartan cilexetil) by GC–MS/MS (triple-quad) on **VF-WAXms (G16)** 30 m x 0.25 mm x 1.0 µm.

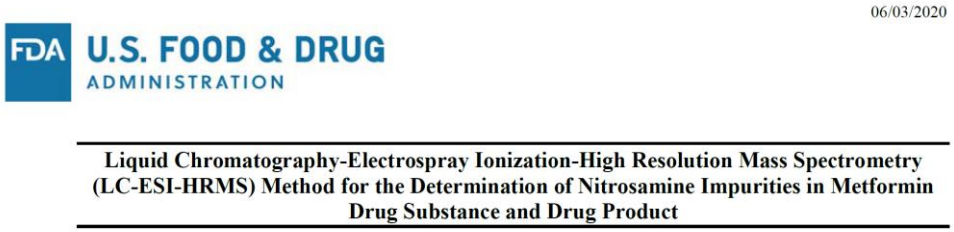
NOTE: ALL published methods use MS for the low-level detection required

FDA Methods

- FDA has published several methods, including 2 on PHX columns



HPLC column: Kinetex® 2.6 µm F5 100 Å, 100 x 4.6 mm (Phenomenex, Part No. 00D-4723-E0)



HPLC column: Phenomenex Kinetex® 2.6 µm Biphenyl 100 Å, 150 x 3.0 mm (Part No. 00F-4622-Y0)

NOTE: ALL published methods use MS for the low-level detection required

Nitrosamine Analytical Challenges

- Nitrosamines lack a chromophore
- Low-level (ppb) detection and quant of nitrosamines is required
  - UV detectors (workhorse of Pharma QC labs) are NOT sensitive enough
  - MS detection required
- High concentration of API in drug substance and drug product
- No single or generic method is available
- Chromatographic interference
  - Separation of API from individual nitrosamines is required in drug product and drug substance to enable accurate quantitation

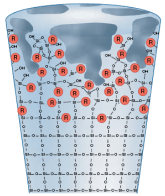
Analyzing Nitrosamines

Nitrosamines are known to be carcinogenic and have the potential to be intermediates in organic synthesis. Due to their potent genotoxicity, nitrosamines have been a serious cause for concern. it has now become a requirement to accurately quantitate this group of compounds in pharmaceuticals during drug development and manufacturing. Below you will find the latest resources to help you improve your LC-MS quantitation of nitrosamines. If you looking to improve your nitrosamine analysis please do not hesitate to contact us.

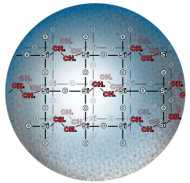
Technique	Brand	Description	Recommended for:
HPLC	Gemini	3 µm C18 150 x 4.6 mm	Ph. Eur. method for N-Nitrosamines in active substances
HPLC	Kinetex	2.6 µm Biphenyl 150 x 3 mm 2.6 µm Biphenyl 150 x 4.6 mm	Sartan drugs, metformin and ranitidine
HPLC	Kinetex	2.6 µm F5 50 x 2.1 mm	Rapid analysis of genotoxic nitrosamines
GC	Zebron	ZB-624*PLUS* 30 m x 0.25 mm x 1.40 µm	Analysis of NDMA and NDEA in sartan drugs
HPLC	Luna Omega	3 µm Polar C18 150 x 3 mm	Nitrosamine impurities in acyclovir

PLC/UHPLC Column Phase Selection Chart

Specifically designed for successful and reproducible method development and transfer



Gemini Twin Technology



Gemini-NX Twin Technology

Gemini columns are rugged reversed-phase HPLC and PREP LC columns that offer extended lifetime at pH 1-12 conditions and excellent stability for reproducible, high-efficiency separations. The Gemini family contains a variety of useful alkyl and phenyl phases bonded to fully porous organo-silica particles.

Gemini® pH Flexible LC

Rugged reversed phase column can be used reliably from pH 1-12

Phase		Particle Type	Pore Size (Å)	Carbon Load %	pH Range	USP Classification	Selectivity Features	Available Particle Size(s)
C18	Hydrophobicity, Steric Interaction, Hydrogen Bond Donating Capacity, Hydrogen Bond Accepting Capacity, **Cation Selectivity at pH 2.8**, **Cation Selectivity at pH 7.0** (Low – High)	Fully Porous Organo-Silica (U.S. Patent Nos. 7,563,367 and 8,658,038)	110	14	1.0 - 12	L1	This is a high loading, organo-silane particle column with pH stability 1-12. The patented procedure creates a surface that is a strong hydrogen donor and accepter. It is ideal for a combination of polar and non-polar retention.	3 µm, 5 µm, 10 µm
NX-C18	Hydrophobicity, Steric Interaction, Hydrogen Bond Donating Capacity, Hydrogen Bond Accepting Capacity, **Cation Selectivity at pH 2.8**, **Cation Selectivity at pH 7.0** (Low – High)	Fully Porous Organo-Silica (U.S. Patent Nos. 7,563,367 and 8,658,038)	110	14	1.0 - 12	L1	New generation of organo-silane material incorporates ethylene bridges to provide pH stability from 1-12 and 5x the durability of earlier hybrids. The homogenous surface offers some steric selectivity.	3 µm, 5 µm, 10 µm
C6-Phenyl	Hydrophobicity, Steric Interaction, Hydrogen Bond Donating Capacity, Hydrogen Bond Accepting Capacity, **Cation Selectivity at pH 2.8**, **Cation Selectivity at pH 7.0** (Low – High)	Fully Porous Organo-Silica (U.S. Patent Nos. 7,563,367 and 8,658,038)	110	12	1.0 - 12	L11	This is a very inert phase for great peak shapes of ionized compounds. The planar phenyl rings offer moderate hydrophobic retention and high steric selectivity for structural isomer selectivity.	3 µm, 5 µm

PLC/UHPLC Column Phase Selection Chart

KINETEX Core-Shell Technology

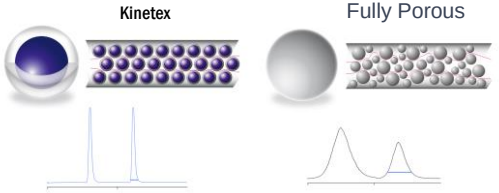
Use for highest performance compared to fully porous media

Phase	Particle Type	Pore Size (Å)	Carbon Load %	pH Range	USP Classification	Selectivity Features	Available Particle Size(s)
EVO C18	Core-Shell Organo-Silica (U.S. Patent Nos. 7,563,367 and 8,658,038)	100	11[a]	1.0-12.0	L1	Robust reversed phase methods even in alkaline conditions with improved peak shape for polar basic compounds and 100% aqueous stability.	1.7 µm 2.6 µm 5 µm
C18	Core-Shell Silica	100	12[a]	1.5-8.5[b]	L1	All purpose phase that offers the hydrophobic retention and methylene selectivity chromatographers expect from a C18 column.	1.3 µm 1.7 µm 2.6 µm 5 µm
Biphenyl	Core-Shell Silica	100	11[a]	1.5-8.5[b]	L11	100% aqueous stable and allows for excellent reversed phase retention and enhanced polar and aromatic selectivity.	1.7 µm 2.6 µm 5 µm
XB-C18 (C18 with protective iso-butyl side chains)	Core-Shell Silica	100	10[a]	1.5-8.5[b]	L1	Unique C18 phase that yields increased hydrogen bonding with hydrophobic selectivity, resulting in improved peak shape for basic compounds and increased retention of acidic compounds.	1.7 µm 2.6 µm 3.5 µm 5 µm
F5 (pentafluorophenyl propyl)	Core-Shell Silica	100	9[a]	1.5-8.5[b]	L43	Highly reproducible pentafluorophenyl propyl phase that offers a unique combination of polar, hydrophobic, aromatic, and shape selectivity.	1.7 µm 2.6 µm 5 µm
C8	Core-Shell Silica	100	8[a]	1.5-8.5[b]	L7	USP L7 phase that provides less hydrophobic and methylene selectivity than a C18.	1.7 µm 2.6 µm 5 µm
Phenyl-Hexyl	Core-Shell Silica	100	11[a]	1.5-8.5[b]	L11	Reversed phase chemistry that allows for greater retention and separation of aromatic hydrocarbons.	1.7 µm 2.6 µm 5 µm
HILIC (Unbonded silica)	Core-Shell Silica	100	0	2.0-7.5	L3	Unbonded silica phase for HILIC conditions to provide selectivity for polar compounds.	1.7 µm 2.6 µm 5 µm

Hydrophobicity
Steric Interaction
Hydrogen Bond Donating Capacity
Hydrogen Bond Accepting Capacity
Cation Selectivity at pH 2.8
Cation Selectivity at pH 7.0
Low — High

[a] Effective Carbon Load. [b] pH range is 1.5-10 under isocratic conditions. pH range is 1.5-8.5 under gradient conditions.

Kinetex Core-Shell Technology delivers dramatic improvements in efficiency over conventional fully porous media, which can be leveraged to increase resolution, greatly improve productivity, reduce solvent consumption, and decrease costs.



Using sol-gel processing techniques that incorporate nano-structuring technology, a durable, homogeneous porous shell is grown on a solid silica core to create a Kinetex Core-Shell particle. This particle morphology results in less band broadening for all four sources of UHPLC band broadening compared to fully porous particles and thus delivers extremely high efficiencies.

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LUNA

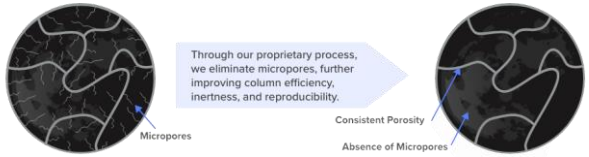
One of the world's leading HPLC/UHPLC columns for virtually every application

Phase	Particle Type	Pore Size (Å)	Carbon Load %	pH Range	USP Classification	Selectivity Features	Available Particle Size(s)
Omega C18	Thermally Modified Fully Porous Silica	100	11	1.5-8.5[A]	L1	Rugged and highly efficient C18 with strong focus on hydrophobic retention of non-polar and polar compounds	1.6µm
Omega Polar C18	Thermally Modified Fully Porous Silica	100	9	1.5-8.5[A]	L1	100% aqueous stability and enhanced selectivity/retention for polar analytes without diminishing useful non-polar retention. The C18 ligand provides general hydrophobic interactions while a polar modified particle surface provides enhanced polar compound retention.	1.6µm 5µm
Omega PS C18	Thermally Modified Fully Porous Silica	100	9	1.5-8.5[A]	L1	Unique, 100% aqueous stable mixed-mode phase that provides both polar and non-polar retention. The surface contains a positive charged ligand which aids in the retention of acidic compounds through ionic interactions, while the C18 ligand promotes general reversed phase retention. The positively charged surface also improves basic compound peaks shape through ionic repulsion.	1.6µm 5µm
C18(2)	Fully Porous Silica	100	17.5	1.5-9.0[B]	L1	Excellent general purpose reversed phase selectivity with high hydrophobic and methylene retention. Non-polar endcapping virtually eliminates silanol interactions.	2.5µm 3µm 5µm 10µm
C8(2)	Fully Porous Silica	100	13.5	1.5-9.0[B]	L7	General C8 phase that provides less hydrophobic retention than a C18, but the density of the ligand bonding creates more steric based selectivity.	3µm 5µm 10µm
CN	Fully Porous Silica	100	7	1.5-7.0	L10	Can be used as reversed or normal phase material. Nitrile groups bound to the silica surface offer a unique polar selectivity under reversed phase or normal phase conditions.	3µm 5µm 10µm
HILIC (cross-linked diol)	Fully Porous Silica	200	5.7	1.5-8.0	L20	HILIC phase that provides excellent selectivity and retention for polar compounds as well as improved MS sensitivity with low bleed.	3µm 5µm
NH_2	Fully Porous Silica	100	9.5	1.5 - 11	L8	Amino phase. Can be used in reversed or normal phase modes. Stable from pH 1.5 to 11.0 and under 100% aqueous conditions. High performance silica and bonding techniques produces a rugged, highly reproducible column.	3µm 5µm 10µm
PFP(2)	Fully Porous Silica	100	11.5	1.5-8.0	L43	A pentafluorophenyl phase that provides excellent selectivity for aromatic compounds from influence of fluorine substitution on phenyl ring. Multiple retention mechanisms. Orthogonal selectivity to traditional C18 phases.	3µm 5µm
Phenyl-Hexyl	Fully Porous Silica	100	17.5	1.5-9.0[B]	L11	A phenyl phase which employs a hexyl alkyl linker; leading to a balanced degree of hydrophobic and aromatic selectivity. Our most hydrophobic phenyl column and it will also provide good hydrogen accepting functionality for acidic retention.	3µm 5µm 10µm
SCX	Fully Porous Silica	100	0.55% Sulfur Load	2.0 - 7.0	L9	A benzene sulfonic acid bonded phase is used to make this strong cation exchange (SCX) column. Offers great peak shape and resolution.	5µm 10µm
Silica(2)	Fully Porous Silica	100	0	2.0 - 7.5	L3	Ultra-pure silica with high column bed stability enhanced by particle shape uniformity.	3µm 5µm 10µm

Hydrophobicity
Steric Interaction
Hydrogen Bond Donating Capacity
Hydrogen Bond Accepting Capacity
Cation Selectivity at pH 2.8
Cation Selectivity at pH 7.0
Low — High

Luna Omega Silica

One of the world's leading HPLC brands, now enhanced for incredible HPLC and UHPLC performance! Luna Omega 1.6, 3, and 5 µm columns culminate 20 years of technological prowess, advancements, and innovation from Phenomenex! With astounding efficiency levels, highly versatile selectivities, and trusted accuracy, Luna Omega columns will take your chromatographic experience to a new level.



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TN-1334

Sensitive and Reproducible Quantification of N-Nitroso Propranolol in a Propranolol Drug Substance and Product

Pankaj Partani[1], Sandeep Choudhary, PhD[1], Preeti Bharatiya[1], Upendra Gunta[1], Ranjith Kumar Ponnamaneni[1], Manoj Pillai, PhD[1], Rahul Baghla[2], Eshani Nandita, PhD[2], and Bryan Tackett, PhD[3]
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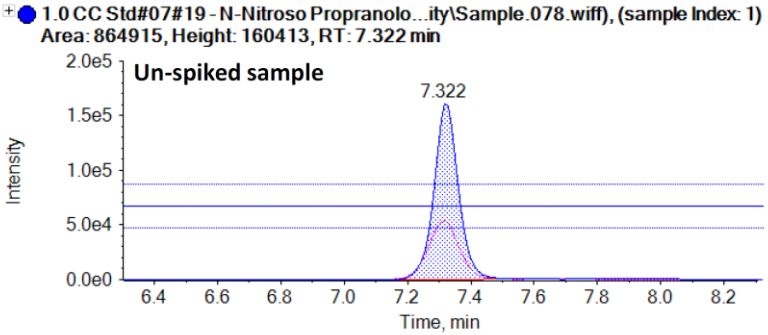
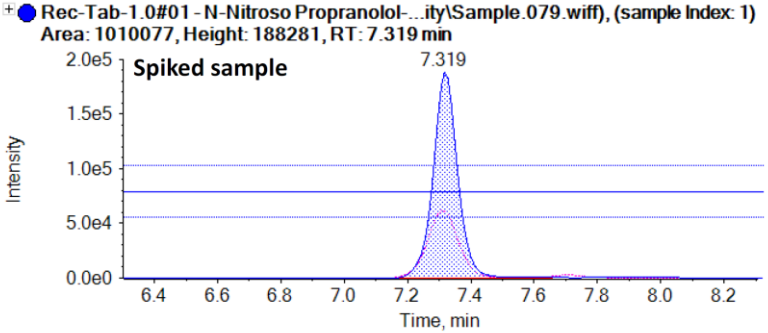
[3]Phenomenex Inc., 411 Madrid Ave., Torrance, CA 90501, USA





LC Conditions

Column: Kinetex™ 2.6 µm Biphenyl
Dimensions: 150 x 3.0 mm
Part No.: 00F-4622-Y0
Mobile Phase: A: 1 mM Ammonium Formate with 0.1 % Formic Acid in Water
B: 0.1 % Formic Acid in Acetonitrile

Gradient:

Time (min)	%B
0.00	35
3.00	35
5.00	55
6.00	75
8.00	75
8.10	95
10.0	95
10.1	35
14.0	35

Flow Rate: 0.4 mL/min
Injection Volume: 15 µL
Temperature: 40 °C
LC System: SCIEX ExionLC™
Detection: MRM
Detector: SCIEX QTRAP 6500+

TN-1335

Low-level Quantification of 10 Mutagenic Nitrosamine Impurities in Acyclovir

Lakshmanan Deenadayalan[1], Sashank Pillai[1], Rahul Baghla[2], Elliot Jones[2], Eshani Nandita, PhD[2], and Bryan Tackett, PhD[3]
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[2]AB Sciex LLC, 500 Old Connecticut Path, Framingham, MA 01701, USA
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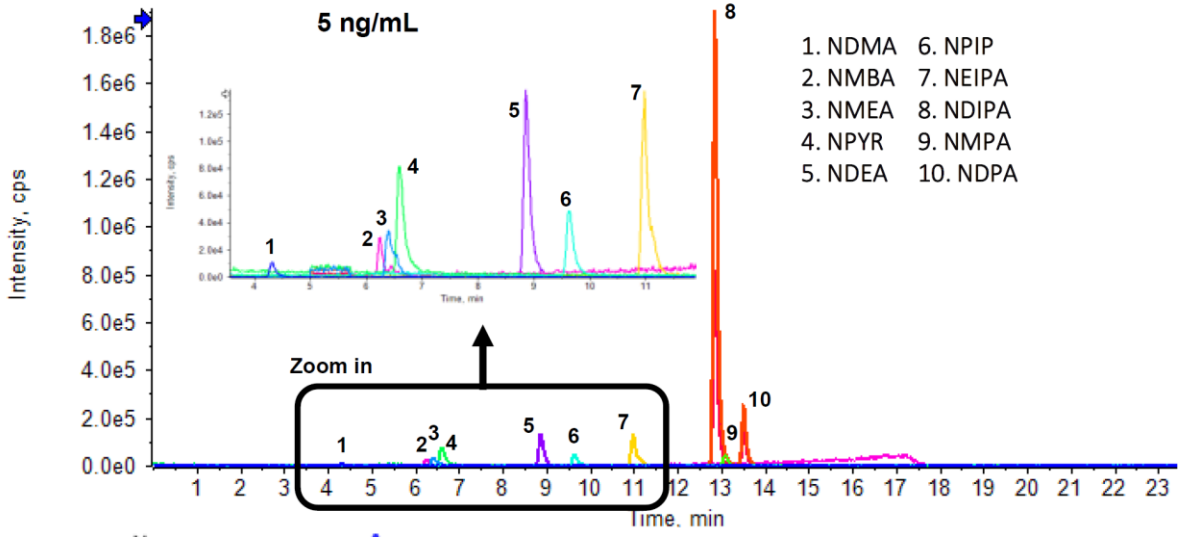


LC Conditions

Column:	Luna™ Omega 3.0 µm Polar C18
Dimensions:	150 x 3.0 mm
Part No.:	00F-4760-Y0
Mobile Phase:	A: 0.1 % Formic Acid in Water B: 0.1 % Formic Acid in Methanol

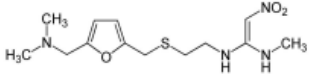
Gradient:	**Time (min)**	**%B**
	0.00	2
	1.00	2
	20.0	98
	22.0	98
	22.1	2
	24.0	2

Flow Rate:	0.45 mL/min
Injection Volume:	20 µL
Temperature:	35 °C
LC System:	SCIEX® ExionLC™
Detection:	MRM
Detector:	SCIEX QTRAP® 6500+

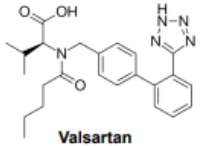
LC-MRM-MS Method for the Detection and Quantificationof Six Nitrosamine Impurities in Sartan (ARBs) Drugs

Introduction

Angiotensin II receptor blocker drugs (ARBs) are widely used to lower high blood pressure. Genotoxic Nitrosamine impurities were first discovered in various sartan drugs in 2019. Since then, several other drugs (for example, Metformin, Ranitidine, Valsartan, and Acyclovir) have been subjected to recall due to the presence of nitrosamine impurities; and regulatory agencies such as FDA and EMA have required manufacturers to conduct a risk assessment, and test for Nitrosamines.



Ranitidine



Valsartan

Due to the potential genotoxicity of Nitrosamines, and the challenge to detect and quantitate these polar impurities, sensitive LC-MS/MS methods must be developed. Here we describe a LC-MRM-MS method for the detection and quantification of six N-Nitrosamine (NDMA, NDEA, NMBA, NEIPA, NDBA, NDPA) impurities at sub-ppm levels in drug substances using a SCIEX® API 4000™ Triple Quad™ mass spectrometer and reversed phase HPLC using columns with different selectivities.

Materials and Methods

Reagents and Sample Preparation

Analytical reference standards were purchased from Sigma-Aldrich® Company (St. Louis, MO, USA). Drug substances were purchased from USP. Drug substances were spiked with various concentrations obtained by serial dilution of a stock solution containing all six nitrosamines to obtain a suitable linear range of detection for the different drugs. MultiQuant™ software was used for qualitative and quantitative purposes.

LC Conditions

Column: Kinetex 2.6 µm F5, 100 x 3.0 mm (00D-4723-Y0)
Kinetex 2.6 µm Biphenyl, 100 x 4.6 mm (00D-4622-E0)
Luna Omega 3 µm Polar C18, 100 x 4.6 mm (00D-4760-E0)

Mobile Phase: A: 0.1 % Formic Acid in Water
B: 0.1 % Formic Acid in Methanol

Gradient:

Kinetex F5			Kinetex Biphenyl			Luna Omega Polar C18		
Time (min)	%B	Flow Rate	Time (min)	%B	Flow Rate	Time (min)	%B	Flow Rate
0	20	0.4 mL/min	0	20	0.55 mL/min	0	2.5	0.4 mL/min
1.97	55	0.4 mL/min	1.97	55	0.55 mL/min	2	2.5	0.4 mL/min
5.54	55	0.4 mL/min	5.54	55	0.55 mL/min	7	50	0.4 mL/min
5.57	90	0.4 mL/min	5.57	90	0.55 mL/min	7.01	50	0.4 mL/min
6.97	90	0.4 mL/min	6.97	90	0.55 mL/min	12	97.5	0.4 mL/min
7	20	0.4 mL/min	7	20	0.55 mL/min	12.9	97.5	0.4 mL/min
13	20	0.4 mL/min	13	20	0.55 mL/min	13.15	2.5	0.4 mL/min
						15	2.5	0.4 mL/min

Injection Volume: 4 µL 4 µL 20 µL
Temperature: 40 °C
LC System: Agilent® 1260 Infinity
Detection: MRM
Detector: SCIEX API 4000 Triple Quad

MRM Conditions

Source: APCI Probe
Polarity: Positive
Source Temperature: 250 °C
GS1: 50 psi
GS2: 30 psi
CUR: 40 psi
CXP: 10
EP: 10
Current: 2

Table 1. MRM Transitions and Parameters.

Analyte	Q1 (Da)	Q3 (Da)	DP (V)	CE (V)
N-Nitrosomethylaminobutyric Acid (NMBA) 1	147	117	28	10
N-Nitrosomethylaminobutyric Acid (NMBA) 2	147	87	28	17
N-Nitrosodiisopropylamine (NDIPA) 1	131	43	35	22
N-Nitrosodiisopropylamine (NDIPA) 2	131	89	35	12
N-Nitrosodimethylamine (NDMA) 1	75	58	55	17
N-Nitrosodimethylamine (NDMA) 2	75	43	55	23
N-Nitrosodibutylamine (NDBA) 1	159	57	38	21
N-Nitrosodibutylamine (NDBA) 2	159	103	38	15
N-Nitrosodiethylamine (NDEA) 1	103	75	50	17
N-Nitrosodiethylamine (NDEA) 2	103	47	50	26
N-Nitrosoethylisopropylamine (NEIPA)	117	75	30	14

LC-MRM-MS Method for the Detection and Quantificationof Six Nitrosamine Impurities in Sartan (ARBs) Drugs

Results

Figure 1. Representative Chromatogram of 6 Nitrosamine Impurities Using a Kinetex 2.6 µm F5 Column.

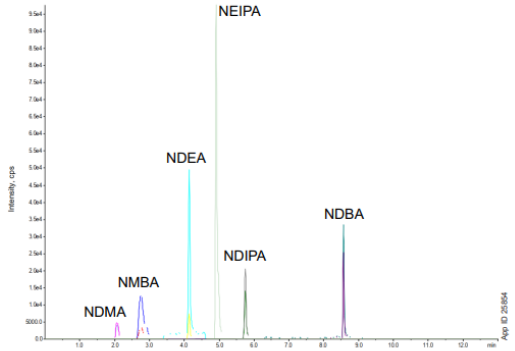


Figure 2. Representative Chromatogram of 6 Nitrosamine Impurities Using a Kinetex 2.6 µm Biphenyl Column.

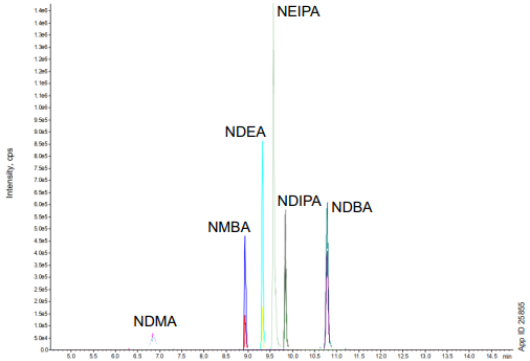


Figure 3. Representative Chromatogram of 6 Nitrosamine Impurities Using a Luna Omega 3 µm Polar C18 Column.

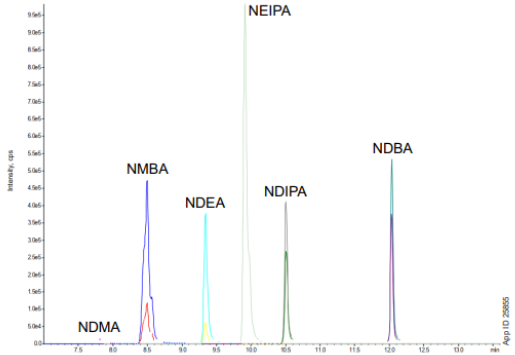


Figure 4. Calibration Curve for the Six Nitrosamines Impurities Using a Kinetex 2.6 µm F5 Column. Calibration Range is from 0.5 to 25 ng/mL with Correlation Coefficient >0.980 and LOD of 0.007 ppm.

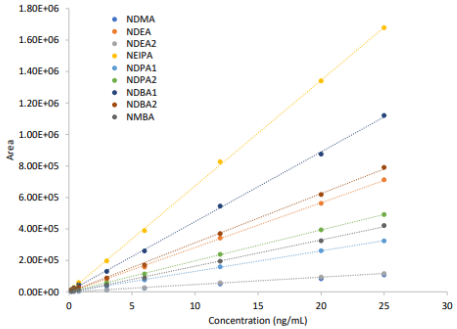


Figure 5. Calibration Curve for the Six Nitrosamines Impurities Using a Kinetex 2.6 µm Biphenyl Column. Calibration Range is from 0.5 to 25 ng/mL with Correlation Coefficient >0.998 and LOD of 0.005 ppm.

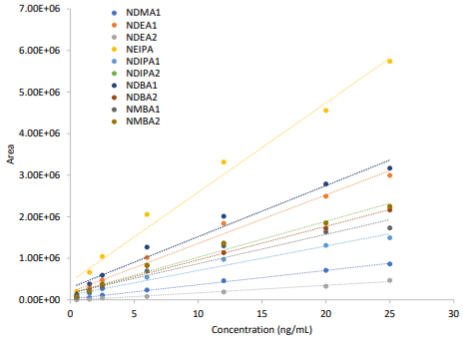
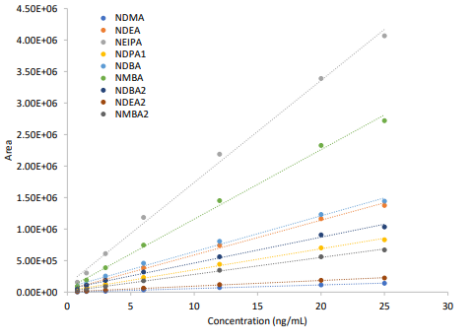


Figure 6. Calibration Curve for the Six Nitrosamines Impurities Using a Luna Omega 3 µm Polar C18 Column. Calibration Range is from 0.5 to 25 ng/mL with Correlation Coefficient >0.980 and LOD of 0.005 ppm.



LC-MRM-MS Method for the Detection and Quantificationof Six Nitrosamine Impurities in Sartan (ARBs) Drugs

Results

Figure 7. % Recovery of Nitrosamine Impurities Spiked in 100 mg/mL Valsartan Using a Kinetex 2.6 µm F5 Column. Recovery of three replicates fell between 100 and 202 % with %RSD between 1.40 and 12.5 %.

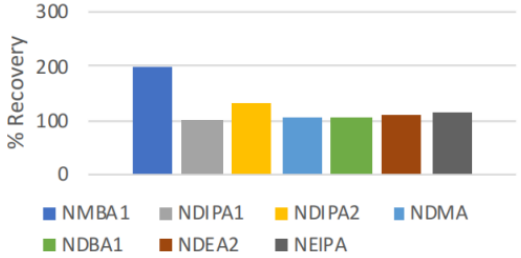


Figure 8. % Recovery of Nitrosamine Impurities Spiked in 100 mg/mL Valsartan Using a Kinetex 2.6 µm Biphenyl Column. Recovery of three replicates fell between 110 and 135 % with %RSD between 18.5 and 5.6 %.

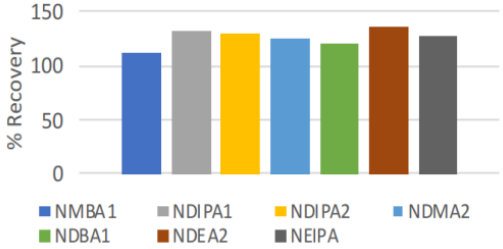
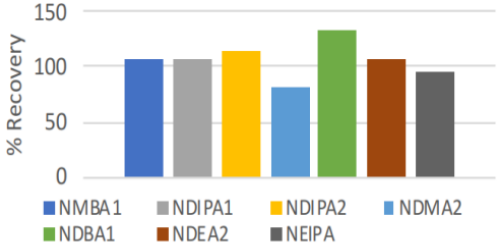


Figure 9. % Recovery of Nitrosamine Impurities Spiked in 100 mg/mL Valsartan Using a Luna Omega 3 µm Polar C18 Column. Recovery of three replicates fell between 100 and 202 % with %RSD between 1.40 and 12.5 %.



Discussion

Conventional C18 columns provide little interaction and retention for small, highly polar compounds. Nitrosamines are compounds of low molecular weight and high polarity, thus making chromatographic separation a challenge. It is important for the column to be capable of retaining the polar Nitrosamines without generating secondary interactions. Secondary interactions can affect peak shape with issues such as tailing or reduced peak height. In turn, this will impact the sensitivity and quantitation of the analytical method.

Conclusion

Here, we present LC-MRM-MS methods capable of detecting highly polar Nitrosamines at 0.007 ppm in the drug product, which is lower than the specification limit for NDMA. Three different stationary phases, a highly inert pentafluoro phenyl, an aqueous stable biphenyl, and a Polar C18 phase, capable of providing excellent retention of polar Nitrosamines with good peak shape, were used for this purpose.

Phenomenex & SCIEX Tech Notes

- TN-1259: Rapid Analysis of Genotoxic Nitrosamines by HPLC-MS/MS
- TN-1265: LC-MS/MS Quantitative Analysis of NDMA in Ranitidine using Kinetex Biphenyl
- Quantification of genotoxic nitrosamines in a telmisartan drug product
- Rapid analysis of genotoxic nitrosamines by HPLC-MS/MS
- Nitrosamine analysis in a pioglitazone drug product
- Rapid method for quantifying nitrosamine compounds with qualitative confirmation
- Analysis of nitrosamine impurities in a metformin drug substance and drug product
- Precise and accurate quantification of nitrosamine impurities in an esomeprazole API
- Varenicline nitrosamine drug substance-related impurity (NDSRI) quantification in a varenicline drug product
- LC-MRM-MS Method for the Detection and Quantification of Six Nitrosamine Impurities in Sartan (ARBs) Drugs
- Robust Analysis of Nitrosamines in a Losartan Drug Substance using Strata™ Activated Carbon Extraction

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