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Original Article

DEVELOPMENT AND VALIDATION OF AN LC-MS/MS METHOD FOR NITROSAMINE IMPURITY DETECTION IN TAMSULOSIN HYDROCHLORIDE

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ABSTRACT

Objective: Regulatory oversight of pharmaceuticals containing nitrosamine contaminants has intensified in the past few years. Unites States Food and Drug Administration (USFDA), European Medicines Agency (EMA) and other regulatory agencies has been quite proactive in sending out warnings, instructions, and safety messages. This study presents a fast, accurate, and selective way to detect and quantify nitrosamine contaminants in Tamsulosin HCl.

Methods: The purification of Tamsulosin using Di Methyl Formamide (DMF) requires monitoring to avoid nitrosamine formation. A 150 × 4.6 mm Symmetry® C18 column (5 µm, 40±1 °C) was used with a mobile phase involving water (98%), acetonitrile (2%) with 0.1% formic acid, where flow velocity was 0.8 ml/min and 10 µl** injection volume. After 1.20 min, the mobile phase composition gradually changed to 90% B (acetonitrile) and 10% A (water). Chromatographic separation took 10 min with a 5±0.5 °C auto-sampler temperature. Atmospheric Pressure Chemical Ionization (APCI) in positive ion mode, with clustering potentials of 36–50 V and collision energy of 9–30 eV, was used for quantification.

Results: Following International Conference Harmonization (ICHQ2R1), showed regression value more than 0.997 and a signal-to-noise ratio of 3.7-4.5 ppm. Approach achieved Limit of Detection (LOD) values over 3.3-12.7 ppm and Limit of Quantification (LOQ) values over 9.9-36.9 ppm, with signal-to-noise ratios greater than 3.7% and greater than 12.9. All of the method recoveries fell between 80% and 120%.

Conclusion: This Liquid Chromatography with Tandem Mass Spectroscopy (LC-MS/MS) technology detects and quantifies nitrosamine impurities in Tamsulosin quickly, sensitively and specifically, assuring regulatory compliance pursuant to USP General chapter<1469>. Impurities in Tamsulosin can be detected at a minimum level using the current technology, which allows for regular analysis.

Keywords: Fragment ion, Tamsulosin, Nitrosamine impurities, APCI (*+ve*)

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INTRODUCTION

Benign Prostatic Hyperplasia (BPH), a condition marked by an enlarged prostate, is primarily treated with the pharmaceutical agent Tamsulosin hydrochloride. It is an alpha-1 blocker, a type of medicine. To facilitate urination, Tamsulosin (fig. 1) relaxes the muscles of the prostate and bladder neck. In these regions, muscular contraction is caused by alpha-1 adrenergic receptors, which are specifically blocked. The possible carcinogenic qualities of nitrosamine impurities have made them a major issue in the pharmaceutical sector [1-3]. To guarantee that pharmaceutical products are safe and effective, it is necessary to create and test analytical methods that can identify and quantify these contaminants with high sensitivity and specificity [4]. Di Methyl Formamide (DMF), preferred for its high yield and purity in Tamsulosin synthesis, requires careful monitoring for nitrosamine formation. Secondary amine cluster in Tamsulosin interacts with dimethyl amine, creating a nitrosamine intermediate, further reacts with DMF in the reaction mixture, producing an assortment of nitrosamine impurities [5, 6]. Removing nitrosamine impurities for human consumption has been highlighted by regulatory agencies like the USFDA and the EMA [7-10]. There are a number of methods that have been published for the determination of Tamsulosin in routine analysis, including UV-spectroscopic [11-20], High-Performance Liquid Chromatography (HPLC) [21-26], LC-MS/MS [27-33], High-Performance Thin Layer Chromatography (HPTLC) [34-38] and others [39-40]. There is not a single one that use LC-MS/MS to detect and quantify potential nitrosamine impurities in Tamsulosin. The purpose of this research is to identify and quantify particular nitrosamine contaminants in Tamsulosin Active Pharmaceutical Ingredient (API) by creating and validating a novel sensitive LC-MS/MS technique, addressing a critical public health concern. In addition to providing a trustworthy analytical tool for guaranteeing the quality and safety of Tamsulosin-based products, the approach seeks to conform to rigorous regulatory standards. This technique is critical amid the increased regulatory scrutiny of nitrosamines and their possible health hazards.

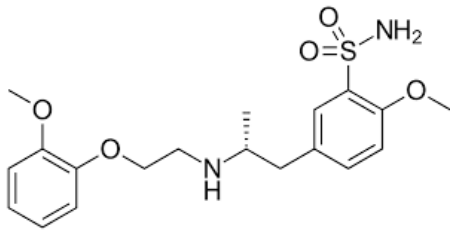


Fig. 1: Molecule of tamsulosin

MATERIALS AND METHODS

Chemicals and reagents

For the making of the mobile phase following USP<621>, analytical grade formic acid from Fluka was used for lowering background noise and any interference. Deployed HPLC grade methanol (lot number DH9DF69917) from Merck and Millipore's Milli-Q water purification device was used to make very clean water, ensures minimum contaminants, offering accurate and trustworthy findings. Sourced entirely from Suven Life Sciences Pvt. Ltd., all of the compounds and experimental materials.

Instruments and equipment

We used high-precision balances that could detect changes as small as 0.01 mg and 0.0001 mg for the weighing process. A Bandelin Sonorex sonicator was used to prepare the samples in the experimental setting. A Symmetry® C18 column with length and I. d of 150 x 4.6 mm and a particle size of 5 µm was used to accomplish the chromatographic separation. A SCIEX 6500+LC-MS/MS system, in conjunction with a Shimadzu Nexera X2, was used to perform the mass spectrometric analysis.

Mobile phase preparation

First mobile Phase (A): Preparation of a solution containing 0.1% formic acid: Combined 1 ml of formic acid with 1000 milliliter of Milli-Q Water and thoroughly blended the both. Second mobile phase (B) constituted 100% Methanol.

Diluent

0.1% formic acid in a mixture of Methanol and water in a 50:50 volume-to-volume ratio.

Preparation of standard stock A

Add approximately 50 ml of methanol to a 200 ml volumetric flask containing approximately 3.3 mg of NDEA, NDIPA, NMIPA, and NEIPA, sonicated to dissolve, and then filled the flask to volume with methanol. Mixed thoroughly.

Preparation of standard stock B

In a volumetric flask with 50 ml marking, add 3 mg of NDMA and 3 mg of NMBA, then sonicated to dissolve. Add 20 ml of methanol, then filled up to volume with methanol, and mixed thoroughly.

Preparation of standard stock C

Kept 1.6 ml of standard stock solutions A and B into a 100 ml volumetric flask, added diluent until the flask was filled to volume, and mixed.

Preparation of standard solution (33 ppm and 120 ppm with respective to sample)

After transferring 2.0 ml of standard stock C to the volumetric flask, mix in 20 ml of diluent.

Preparation of test solution (0.8 mg/ml)

We transferred approximately 16 milligrams of Tamsulosin hydrochloride API to a 20 milliliter volumetric flask, sonicated it to dissolve it, and then added 15 milliliters of diluent, bringing the total volume to 20 milliliters. We mixed everything thoroughly.

Procedure

Diluent was injected once, followed by six injections of the standard preparation and one injection of the test solution into the LC-MS/MS system. Recorded the chromatograms and measured the peak responses.

LC-MS/MS conditions

To get the best possible impurity elution, an extensive number of trials were conducted. Conditions that were optimized were achieved on a Symmetry® C18 column (150 x 4.6 mm, 5 µm particle size) kept at 40±1.0 °C. Mobile phase injection volume was 10 µl**, and flow rate was 0.8 ml/min with polarity changes. For the first 1.20 min, the mobile phase composition consisted of 98% solvent A (water with 0.1% formic acid) and 2% solvent B (acetonitrile). A gradual change in solvent composition was made, resulting in a mix of 10% solvent A (water with 0.1% formic acid) and 90% solvent B (acetonitrile) after 5.80 min. At last, the system was brought back to its original conditions (98% A, 2% B) at 7.10 min and left to stabilize for 2.90 min before the next injection. The whole chromatographic separation process took ten minutes. Between injections, the auto-sampler was maintained at a temperature of 5±0.5 ℃ and a rinse volume of 1200 µl** was employed, with a dip time of 5 seconds. The APCI source was employed in positive ion mode to detect and quantify target analytes, as it is less prone to ion suppression and simplifies sample preparation [41]. Declustering potentials described by Chidella *et al.* ranged from 36 to 50 V, while entrance potentials were consistently maintained at 10 V for all analytes. Collision energy, a critical factor influencing fragment ion formation, was varied from 9 to 30 eV depending on the specific nitrosamine structure. The collision cell exit potential was adjusted individually for each compound, ranging from 8 to 26 V, to enhance ion transmission and detection sensitivity. These parameters were optimized to ensure high signal-to-noise ratios and detailed fragmentation patterns for each nitrosamine impurity.

System suitability

The purpose is to ensure that the analytical system runs smoothly correctly. Injected the diluent and a standard impurity solution (100%) and took chromatograms. By using the below formulae calculated each impurity in ppm individually.

$$\text{NDEA, NDIPA, NMIPA and NEIPA} = \frac{(\text{Test area} \times W_1 \times 1.6 \times 2 \times 20 \times P)}{(S\tan dard area \times 200 \times 100 \times 20 \times W_T \times 100)} \times 100 \times 10000$$

$$\text{NDMA and NMBA} = \frac{(Test area \times W_2 \times 1.6 \times 2 \times 20 \times P)}{(S\tan dard area \times 50 \times 100 \times 20 \times W_T \times 100)} \times 100 \times 10000$$

Where,

W_1 = Weight of impurity standard NDEA, NDIPA, NMIPA and NEIPA

W_2 = Weight of impurity standard NDMA and NMBA (ppm)

P = Potency of the standard

W_T = Weight of the test sample

Specificity

Analytical methods are considered specific if they can clearly evaluate the analyte even when other components, like contaminants, degradation products, and matrix components, are present. Performed diluent and placebo interference by injecting three diluent solutions. To check the impurities interference injected all individual impurities at specification level.

Precision

Method precision

A homogeneous sample of a single batch is analyzed six times by preparing two test samples and six spiked test samples from a single batch, assesses the similarity of measurement findings acquired under identical circumstances.

Intermediate precision

To make sure that the analytical results won't change, rehearsed the method's precision setting by various analysts on separate days using columns other than precision. Used six samples of a homogeneous final sample, inspects the variability of the analytical approach.

LOD and LOQ

Both were calculated by S/N ratio method.

Linearity and range

Conducted a linearity analysis starting from the LOQ level up to 200% of impurity.

Accuracy

To ensure the precision of the test, samples were prepared by adding impurities to the test solution at concentrations of LOQ, 50%, 100%, and 200% of the target. Except for the LOQ and 200% levels, we prepared three instances of the accuracy samples for every level.

Batch analysis

Prepared standard and test solution as per test procedure.

RESULTS AND DISCUSSION

Method development

Chromatographic retention duration of 4.47, 6.46, 5.15, 6.35, 7.69, and 7.14 min for the target nitrosamine impurities (NDMA, NDEA,

NMBA, NMIPA, and NEIPA) were found. The primary analyte, Tamsulosin, eluted after 5.69 min, Khorolskiy M*etal* method describes on effective resolution of three sartans [42]. We used multiple reaction monitoring (MRM) for mass spectrometric detection. Each molecule has its own unique transitions between the ions that serve as a precursor and a product. Observed ion transitions included NDMA (m/z 75->58), NDEA (m/z 103->47), NMBA (m/z 147.1->117), NMIPA (m/z 103.1->61), NDIPA (m/z 131->89), NEIPA (m/z 117.1->74.8), and Tamsulosin (m/z 409->228.6). The sensitivity and selectivity of each analyte were improved by selecting these particular ion pairs. Distillation served to recover solvents alongside refining experimental techniques.

System suitability

Plate count (A) and tailing factor (B) values for six nitrosamine impurities (NDMA, NDEA, NMBA, NMIPA, NDIPA, and NEIPA) are included in the details supplied in table 1. The plate count values vary from about 2200 to 6900 for the various nitrosamine contaminants, as shown in the plate count (A). Reasonable peak symmetry is indicated by tailing factor (B) values for nitrosamine impurities, which are often less than 2. Having said that, there are a handful of values higher than 1.3, which could indicate a little tailing of the associated peaks on a whole par with ICH Q_2 (R_1).

Specificity

Presenting in table 2 the data are the retention duration of diluent solutions and various nitrosamine impurities (NDMA, NDEA, NMBA, NMIPA, NDIPA, and NEIPA). Since the diluent solutions in fig. 2 did not introduce any unwanted noise or overlapping peaks into the analytical process, the selectivity of the approach is further reinforced as per regulatory guidelines.

Table 1: Results for system suitability

NDMA		NDEA		NMBA		NMIPA		NDIPA		NEIPA	
A	**B**	**A**	**B**	**A**	**B**	**A**	**B**	**A**	**B**	**A**	**B**
6477	0.46	3036	1.43	4346	0.13	3259	0.32	4062	0.67	2271	0.12
6916	0.46	3049	1.43	4622	0.12	3219	0.32	4316	0.67	2270	0.11
5573	0.47	2994	1.44	4658	0.13	3156	0.32	3924	0.68	2235	0.12
6417	0.46	3020	1.43	4827	0.12	3209	0.32	3825	0.67	2219	0.11
5121	0.46	2956	1.43	4722	0.13	3161	0.32	3881	0.67	2197	0.12
5878	0.46	2949	1.44	4755	0.13	3133	0.32	3874	0.68	2238	0.12
6064± 661.2	0.46±0.0	3001±41.6	1.43±0.0	4655± 661.2	0.13±0.0	3189±47.3	0.32±0.0	3980± 183.2	0.67±0.0	2238±28.9	0.12±0.0
4.1˙	0.1˙	1.4˙	0.1˙	3.6˙	0.1˙	1.5˙	0.0˙	1.3˙	0.1˙	1.3˙	0.1˙

A-USP Count; B-Tailing Factor**;** n=6 replicates for each impurity, data presented in (mean±SD);˙ % Relative standard deviation

Table 2: Results for blank, impurity interference and RT confirmation

Impurity/Name of solution	Retention time of individual solution▲	Interference observed (Yes/No)
Diluent solution-1	-	No
Diluent solution-2	-	No
Diluent solution-3	-	No
NDMA	4.46	No
NDEA	6.43	No
NMBA	5.13	No
NMIPA	6.31	No
NDIPA	7.67	No
NEIPA	7.11	No

▲in min

Precision

The findings presented in tables 3 and 4 show an usually acceptable level of precision in retention time and peak area measurements is indicated by the extremely narrow range of percent relative standard deviation (%RSD) values for all contaminants, which range from 0.0% to 0.1% and from 0.1% to 1.5%, respectively. Recovery rates align with reported values in previous nitrosamine studies by Gopireddy *et al.*, ensuring the method's reliability. Excellent repeatability in peak area response is suggested by the lower %RSD values of 0.1–0.4% for NDMA, NDEA, NMBA, and NEIPA. The moderate amount of variability in peak area measurements for NMIPA and NDIPA is shown by slightly higher %RSD values of 1.3% and 1.5%, respectively. The level of contaminants was determined to be not detected in the unspiked preparations. Nitrosamine impurities (NDMA, NDEA, NMBA, NMIPA, NDIPA, and NEIPA) in six spiked test samples (SI-1 to SI-6) are computed in ppm. All contaminants have acceptable %RSD values of 0.0% to 5.5%inline to<1469>. Implications exhibited good precision in assessing spiked samples' nitrosamine impurity concentrations. NDMA, NDEA, NMIPA, and NDIPA have good concentration consistency with %RSD values between 1.3% and 2.3% as that of reported by Tuna Öncü *et al.* for sartan groups [43]. NMBA has the greatest %RSD (5.5%) of all contaminants, indicating higher quantification variability.

Table 3: Results for RT in system precision

Retention time (min)					
NDMA	**NDEA**	**NMBA**	**NMIPA**	**NDIPA**	**NEIPA**
4.46	6.43	5.13	6.32	7.67	7.12
4.46	6.43	5.12	6.32	7.67	7.11
4.47	6.44	5.13	6.32	7.68	7.12
4.46	6.43	5.12	6.32	7.67	7.11
4.46	6.43	5.13	6.32	7.67	7.12
4.46	6.44	5.13	6.32	7.68	7.12
4.46±0.004	6.43±0.005	5.13±0.005	6.32±0.000	7.67±0.005	7.12±0.005
0.1˙	0.1˙	0.1˙	0.0˙	0.1˙	0.1˙

n=6 replicates for each impurity, Data presented in (mean±SD); ˙% Relative standard deviation

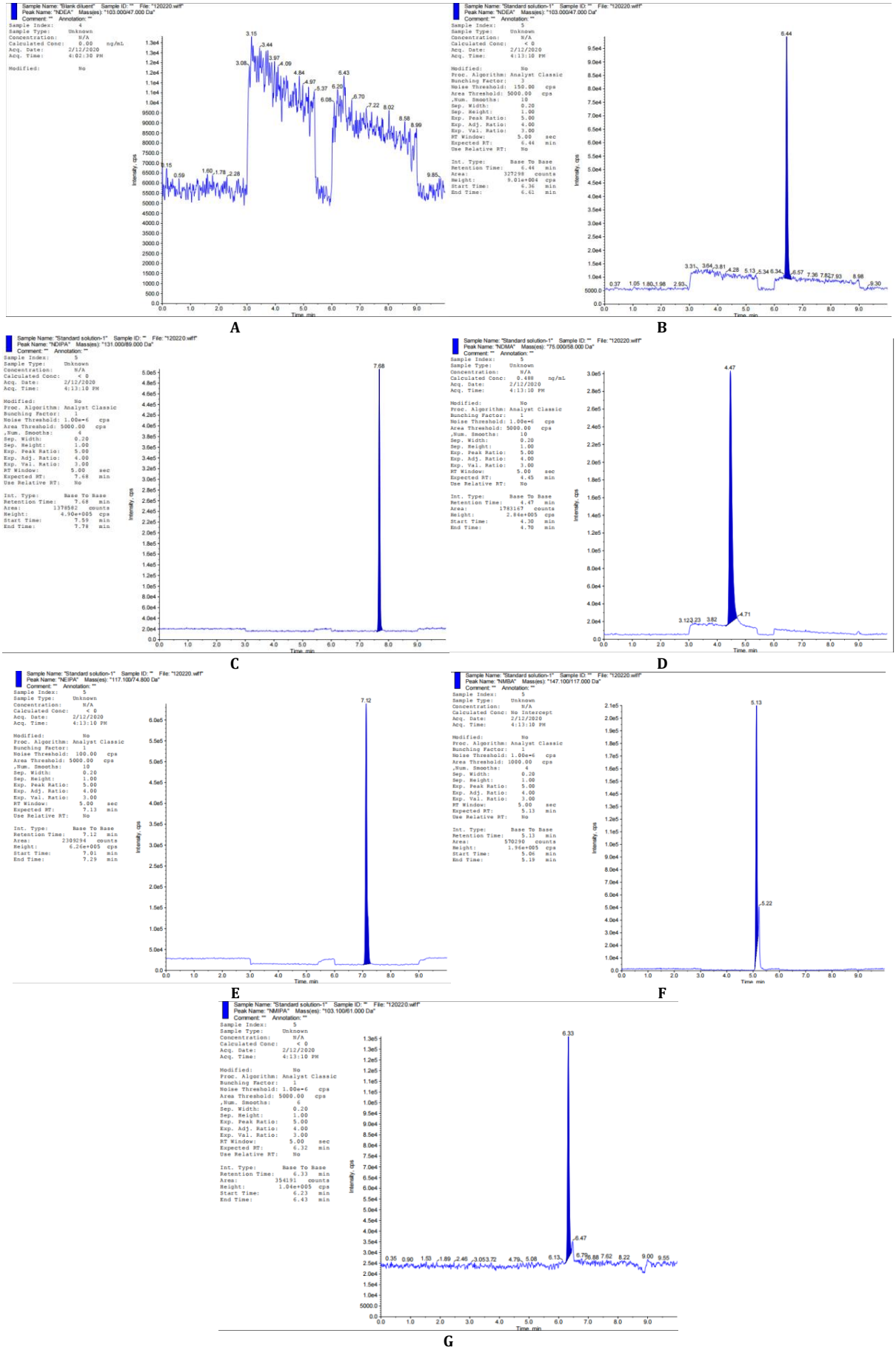


Fig. 2: TIC of impurity standards: A-Blank, B-NDEA, C-NDIPA, D-NDMA, E-NEIPA, F-NMBA, G-NMIPA

Table 4: Results for system precision (Area) in precision

NDMA	NDEA	NMBA	NMIPA	NDIPA	NEIPA
1647757	303671	434681	325926	1406216	2271702
1691634	304948	462296	321984	1431674	2270466
1557334	299437	465872	315609	1392459	2235472
1641760	302053	482776	320981	1382505	2219916
1512148	295655	472255	316179	1388104	2197425
1587889	294911	475502	313317	1387446	2238101
1606420±66119.8	300113±4175.9	465564±16759.0	318999±4744.5	1398067±18338.6	2238847±28862.9
4.1˙	1.4˙	3.6˙	1.5˙	1.3˙	1.3˙

n=6 replicates for each impurity, Data presented in (mean±SD); ˙% Relative standard deviation

Intermediate precision

Tables 5 and 6 show that retention periods and peak area for the six nitrosamine impurities (NDMA, NDEA, NMBA, NMIPA, and NEIPA) were properly recorded across six standard injections, and measurements were accurate since the %RSD values for all pollutants were 0.1% to 0.2% and 0.8% to 5.5%, respectively. In unspiked preparations, pollutants were not found as exhibited.

LOD, LOQ establishment

The analytes with the highest sensitivity were NDEA and NMIPA, which had the lowest values at 3.3 and 3.4 ppm, respectively. NDMA and NMBA have reduced sensitivity, as seen in table 7 by their significantly higher LOD values (12.7 and 12.0 ppm). NDEA and NMIPA show improved quantification capability for these analytes with reduced LOQ values (3.4 and 3.3 ppm, respectively). NDMA and NMBA are less accurately quantified at lower concentrations, as their higher LOQ values (36.9 and 36.5 ppm, respectively) suggest.

Linearity

From table 8, we can see that for NDMA, NDEA, NMBA, NMIPA, NDIPA, and NEIPA, there is a very good linear relationship between the concentration of each impurity and its associated peak area throughout the examined range, wherein Baksam *et al.* reported method for detection of a single nitrosamine impurity [44]. Further evidence as in fig. 3 of strong linearity is the small residual sum of squares, which shows that the data points deviate very little from the regression line, falling inside the bounds.

Table 5: Results for system precision (RT▲) in intermediate precision

NDMA	NDEA	NMBA	NMIPA	NDIPA	NEIPA
4.46	6.44	5.12	6.32	7.67	7.12
4.45	6.43	5.13	6.32	7.67	7.12
4.46	6.43	5.12	6.32	7.68	7.12
4.46	6.44	5.12	6.33	7.68	7.13
4.47	6.45	5.13	6.33	7.69	7.13
4.47	6.44	5.13	6.33	7.68	7.13
4.46±0.0	6.44±0.0	5.13±0.0	6.33±0.0	7.68±0.0	7.13±0.0
0.2˙	0.1˙	0.1˙	0.1˙	0.1˙	0.1˙

n=6 replicates for each impurity, Data presented in (mean±SD); ˙% Relative standard deviation; ▲in min

Table 6: Results for system precision (Area) in intermediate precision

NDMA	NDEA	NMBA	NMIPA	NDIPA	NEIPA
1652277	303522	463893	325027	1395135	2211701
1667913	306973	425434	326151	1435701	2178375
1612793	312075	437059	328741	1417189	2183916
1593795	302188	436684	327325	1415868	2180498
1620847	304510	417343	314462	1355915	2197932
1569719	304288	400026	324028	1397500	2163084
1619557±36342.3	305593±3540.6	430073±21553.2	324289±5092.9	1402885±27368.9	2185918±16856.9
2.2˙	1.2˙	5.0˙	1.6˙	2.0˙	0.8˙

n=6 replicates for each impurity, Data presented in (mean±SD); %RSD; ˙% Relative standard deviation

Table 7: Results for LOD, LOQ Establishment

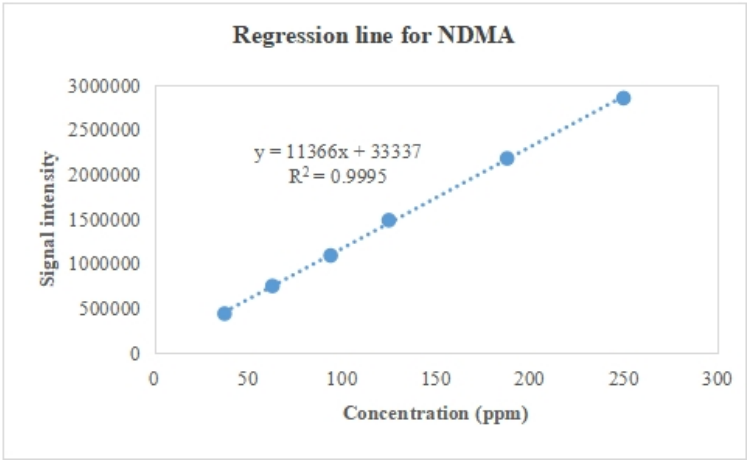
Impurity[a]	LOQ	S/N×	LOD	S/N×
	ppm		ppm	
NDMA	36.9	14.0	12.7	4.7
NDEA	9.9	14.5	3.4	4.5
NMBA	36.5	15.1	12.0	5.4
NMIPA	10.0	12.9	3.3	3.7
NDIPA	9.9	13.0	3.3	3.8
NEIPA	10.1	14.0	3.4	4.6

S/N×-Signal-to-Noise ratio

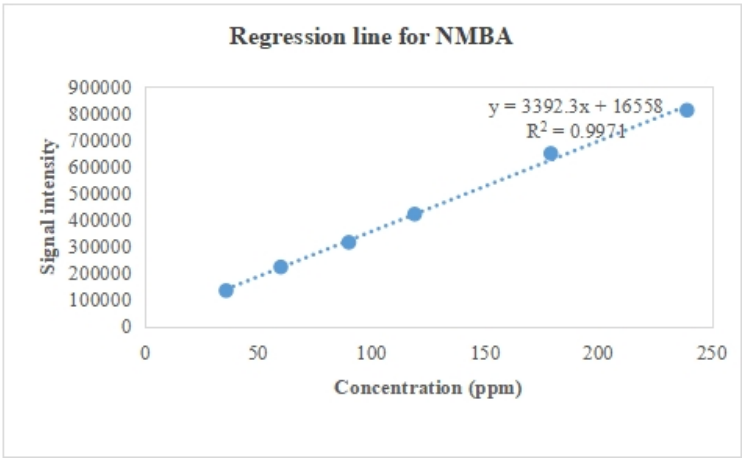
Table 8: Obtained peak areas for linearity of NDMA NDEA, NMBA, NMIPA, NDIPA, NEIPA

C	NDMA	C	NMBA	C	NDIPA	NDEA	NMIPA	NEIPA
37.5	441173	35.9	133738	10	406263	88323	100093	631587
63	751687	60	222328	17	677159	151262	155120	1051749
94	1092881	90	314908	25	1012846	223164	248813	1601192
125	1487907	119	420850	33	1361835	297854	316885	2120967
188	2180313	179	648753	50	2026003	444691	468523	3177403
250	2855765	239	811055	66	2684513	579916	607255	4165458

C-Concentration in ppm



A



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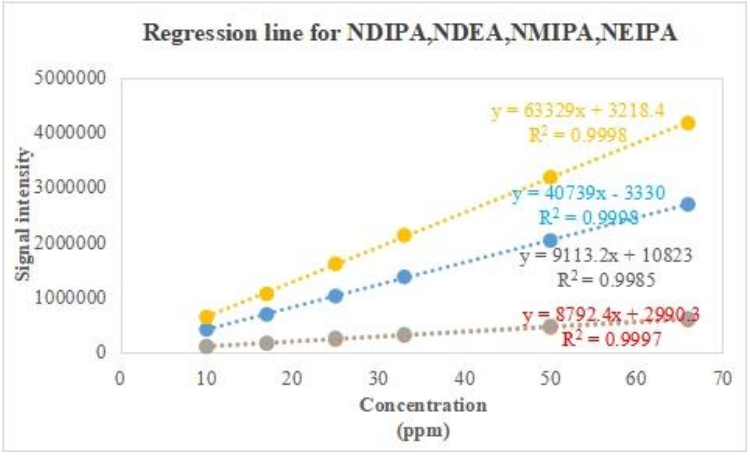

C

Fig. 3: Indicator of concentration-peak response relationship for A-NDMA, B-NMBA, C-NDIPA, NDEA, NMIPA, NEIPA

Accuracy

Most impurity recovery values in Tables 9 are within the 85-115% range, which is considered acceptable and shows that the analytical method is accurate at the LOQ and at 200%level. For this particular contaminant, NDMA shows the lowest recovery values (83.7% to 89.1%) at LOQ level, and (88.4-91.8% and 91.7-96.2%, at 200% level respectively) compared to the other impurities as reported by Gopireddy *et al.* in class of sartans [45]. In comparison, Rao *et al.* [46] reported recoveries of 90–105% and Remidicherla *et al.* [47] demonstrated recoveries of 92–104% for nitrosamine impurities in Doxofylline, aligning with trace-level analysis criteria, the current method demonstrates superior sensitivity. Recoveries for the other impurities (NDEA, NMBA, NDIPA, and NEIPA) are more regular and dependable, falling within a tighter range of 91.2% to 102.4% at LOQ and 92.4-101.8% at 200% level inline to criteria.

Batch analysis

Three separate batches, each with two preparations, were tested for the presence of nitrosamine impurities using the developed and validated method. According to table 10, it was found that there were no impurities.

Table 9: Results for each impurity recovery at LOQ (10 ppm) level

Description	% Recovery					
	NDMA	NDEA	NMBA	NMIPA	NDIPA	NEIPA
Preparation-1	91.8	100.2	97.3	94.8	96.8	97.3
Preparation-2	90.8	96.4	99.8	91.7	96.2	95.8
Preparation-3	88.4	98.6	101.8	96.2	96.6	96.5
Preparation-4	90.6	96.4	95.5	93.5	93.3	96.4
Preparation-5	90.8	97.7	95.9	93.9	92.4	94.0
Preparation-6	88.4	95.3	95.9	94.8	95.0	96.2
Minimum	88.4	95.3	95.5	91.7	92.4	94.0
Maximum	91.8	100.2	101.8	96.2	96.8	97.3

Table 10: Results for batch analysis

Impurity in ppm						
Impurity	Batch A		Batch B		Batch C	
	Prep-1	Prep-2	Prep-1	Prep-2	Prep-1	Prep-2
NDMA	NI▲	NI▲	NI▲	NI▲	NI▲	NI▲
NDEA	NI▲	NI▲	NI▲	NI▲	NI▲	NI▲
NMBA	NI▲	NI▲	NI▲	ND▲	NI▲	NI▲
NMIPA	NI▲	NI▲	NI▲	ND▲	NI▲	NI▲
NDIPA	ND▲	NI▲	NI▲	ND▲	NI▲	NI▲
NEIPA	ND▲	NI▲	NI▲	ND▲	NI▲	NI▲

▲Not Identified/Detected

CONCLUSION

This is the first ultra-sensitive LC-MS/MS approach for detection of nitrosamines within Tamsulosin, achieving lower LOD and LOQ values compared to existing methods. While numerous methods have been published for nitrosamines in various drug substances, none have been developed to quantify nitrosamines in Tamsulosin using LC-MS/MS. We were able to set up all the necessary validation settings to prove the procedure worked. No detectable levels of the six nitrosamine impurities were observed in the tested Tamsulosin batches. As evidence of the method's sensitive performance, the calculated LOQ (9.9-36.9 ppm) and LOD(3.3-12.7 ppm)values are extremely low for all the nitrosamines. For most nitrosamine contaminants, the recovery data shows satisfactory accuracy at the LOQ and at 200% level. At 0.001% (with respect to test) concentration, the six nitrosamine impurities in Tamsulosin can be routinely quantified using the validated method. Investigating potential matrix effects may provide additional insights on method robustness.

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ABBREVIATIONS

Min: Minute; ml: Milli Litre; g: Gram; mg: Milli Gram; µg: Micro Gram; ng: Nano Gram; RSD: Relative Standard Deviation; LOD: Limit Of Detection; LOQ: Limit Of Quantification; LC-MS/MS: Liquid Chromatography Hyphenated With Mass Spectrometry; NDMA: Nitroso Di Methyl Amine; NDEA: Nitroso Di Ethyl Amine; NDIPA: Nitroso Di Iso Propyl Amine; NEIPA: Nitroso Ethyl Iso Propyl Amine; NMBA: Nitroso Methyl Butyric Acid; NMPA: Nitroso Methyl Phenyl Amine; NDBA: Nitroso Di Butyl Amine; ESI: Electron Spray Ionization; API: Active Pharmaceutical Ingredient; S/N: Signal to Noise ratio; USP: United States Pharmacopoeia

AUTHORS CONTRIBUTIONS

SS (Swetha Sri) created the concept, acquired the data, and finished the original draft. AM (Arram Madhavi) procured resources, and NM (Narender Malothu) corrected the data. GC (Guntupalli Chakravathi) oversaw the study. All authors contributed to the completion of the manuscript.

CONFLICTS OF INTERESTS

This study has no competing interests

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