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DEVELOPMENT AND VALIDATION OF STABILITY INDICATING HPLC METHOD FOR QUANTITATIVE DETERMINATION OF RELATED SUBSTANCES PRESENT IN ELETRIPTAN HYDROBROMIDE DRUG SUBSTANCE

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Keywords:

Eletriptan hydrobromide, Development, Validation Related substances,

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ABSTRACT: An efficient and sensitive RP-HPLC method was developed and validated for the estimation of related substances in Eletriptan hydrobromide drug substance which were identified and characterized by LCMS, FTIR, ^{1}HNMR, ^{13}CNMR techniques. The method was carried out on a Purosphere STAR RP-8e column at temperature 20°C using a phosphate buffer at pH 4.0 and solvent mixture consists of acetonitrile, water and tetrahydrofuran in the ratio of 70:30:1v/v/v in gradient mode of pump. The flow rate is 1.5 ml/min and detection was done at 225nm.The developed RP HPLC method was validated by testing specificity, precision, detection limit, quantification limit, linearity, accuracy, robustness and range. The linearity of the method was confirmed over the range of 0.09 to1.4µg/ml for related substances with correlation coefficients greater than r = 0.999. The accuracy of the method was found to be 98.6 to 102.3% and RSD as found to be less than 2.0% indicating high degree of accuracy and precision for the proposed method. The effective recovery and lower %RSD prove the highness of the proposed RP HPLC method for the routine determination of Eletriptan hydrobromide related substances in drug substance.

INTRODUCTION: Eletriptan Hydrobromide is described chemically as (R) – 5-[2(phenylsulfonyl) ethyl]-3-(N-methylpyrrolidin-2-ylmethyl)-1 H-indole. It is an antimigraine agent and belongs to 5-hydroxytryptamine-1 (5-HT_1) receptor agonist pharmacologic class**.**

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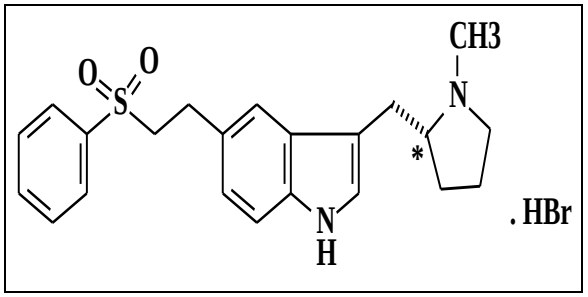
Eletriptan Hydrobromide binds with serotonin 5-HT_{1B} receptors on intracranial blood vessels and serotonin 5-HT_{1D}receptors on sensory nerve endings, constricting cranial arteries and thereby relieving migraine[1]. Its pharmacological effects include the constriction of cerebral blood vessels and neuropeptides secretion blockade which eventually relieves the pain [2]. Eletriptan hydrobromide also inhibits the sensation of tightness, pain, pressure and heaviness in the precordium throat and jaws [3]. Both the United States Pharmacopoeia (USP) and the European

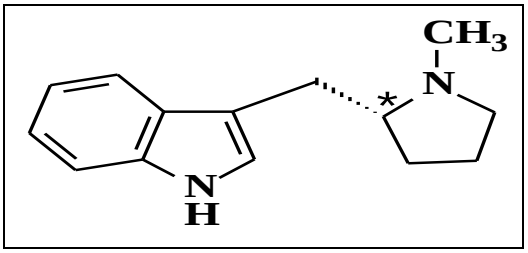
Pharmacopoeia (EP) have not published monographs for this drug substance. However, many of analytical methods have been reported in the literature for the determination of Eletriptan hydrobromide and/or its related substances / impurities. Mirazeceivic and etal [4] published HPLC methodology for quantifying unknown impurity by using X-Terra C_{18} (150mm x 4.6 mm), 5µ column. In 2010, D Suneetha and etal [5] published RP-HPLC method for estimation of Eletriptan hydrobromide in pharmaceutical dosage forms. A validated UPLC method [6] has been reported for the determination of this drug and its process-related impurities. Separation was achieved with Halo C18, 50mm x 4.6 mm, 2.7µm column and also few of the spectroscopic and fluorometric methods are available in literature [7-8].

Analytical Chemistry Insights journal publishes TLC method for quantifying Eletriptan hydrobromide [9]. However, present research work was to develop a suitable stability indicating gradient HPLC method for the determination of Eletriptan hydroromide related substances **Fig 1**, further it was validated with respect to specificity, limit of detection and quantification LOQ linearity, precision, accuracy, robustness and forced degradation and stress studies.

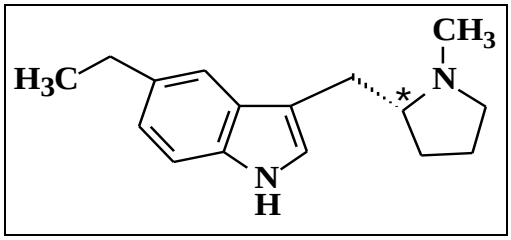
The stress studies of the drug substance can guide to indicate the likely degradation impurities of the products which can in turn help to establish degradation path ways and the intrinsic stabilities of the molecule and validated the stability indicating power of the analytical procedure used. The validated stability method indicates HPLC method was followed in accordance with ICH guidelines [10]. The developed and validated method was applied for the routine analysis of the Eletriptan hydrobromide related substances present in the drug substance.



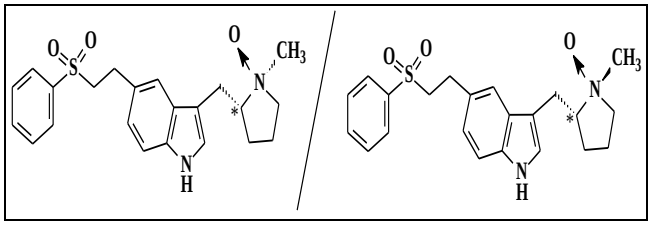
ELETRIPTAN HYDROBROMIDE



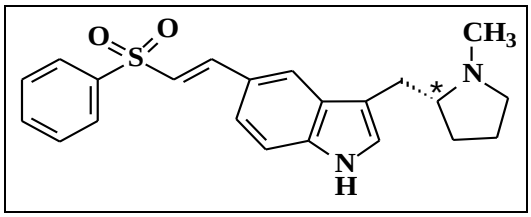
IMPURITY-I
[DES BROMO INDOLE PROLINE]



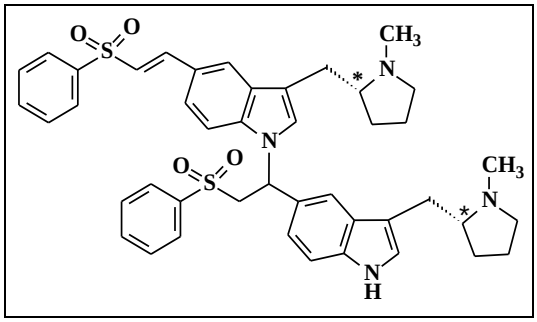
IMPURITY-II
[ETHYL INDOLE PROLINE]



IMPURITY-III
[ELETRIPTAN N-OXIDES]



IMPURITY-IV
[DESACETYL ENE SULFONE DERIVATIVE]



IMPURITY-V
[ELETRIPTAN DIMER]

FIG 1: CHEMICAL STRUCTURES OF ELETRIPTAN HYDROBROMIDE AND ITS RELATED IMPURITIES

Experimental:

Chemicals, Reagents and samples: Eletriptan hydrobromide and its impurities were gifted from

APL Research centre Laboratories (A division of Aurobindo Pharma Ltd., Hyderabad). The Chemical structures of Eletriptan hydrobromide and its related impurities are given in **Fig 1**. Potassium dihydrogen orthophosphate, orthophosphoric acid, acetonitrile, tetrahydrofuran were procured from Merck (India) limited and pure Milli-Q water was prepared with help of Millipore purification system.

High performance liquid chromatography (HPLC): Chromatographic separations were performed on HPLC system with Waters alliance2695 separation module equipped with 2996 photodiode array detector with Empower pro data handling system (Waters Corp., Milford,MA01757,USA). The analysis was carried out on Purosphere STAR RP-8e, 250mm x 4.6mm, 5µ particle size column.

Mobile phase A was phosphate buffer pH 4.0 (prepared by dissolving 6.8g of potassium dihydrogen orthophosphate in 1000ml of water, and pH was adjusted to 4.0 ±0.05 using orthophosphoric acid). Mobile phase B was mixture of degassed acetonitrile, water and tetrahydrofuran in the ratio of 70:30:1 v/v/v. Diluent was prepared by mixing solution of water and acetonitrile in the ratio of 75:25(v/v). Injection volume was 20µl, flow rate was 1.5 ml/min and column oven temperature was 20°C. UV detection was carried out at 225nm and data acquisition time was 50 min. The gradient programme was as follows:

Time (min)/A(v/v):B(v/v); T0.01/75:25, T30/60:40, T40/35:65, T50/35:65, T52/75:25, T60/75:25.

Preparation of solutions:

Standard solution: A stock solution of Eletriptan (300 µg/mL) was prepared by dissolving appropriate amount of substance in the diluent. Working solution of 0.9µg/mL was prepared from this stock solution for the related substances determination.

Sample solution: Prepared a concentration of 600 µg/ml of sample solution with diluent.

Impurity stock solution: A stock solution of all impurities at 250µg/mL was also prepared in the diluent.

Method validation:

Specificity: Specificity is the capability of the method to measure the analyte response of its potential impurities. The specificity of developed HPLC method for Eletriptan hydrobromide was carried out in the presence of its impurities i.e impurities I to V and also verified the blank interference for the accurate measure of impurities.

As a part of specificity stress studies were carried out for Eletriptan hydrobromide drug substance to prove that stability in degradation carried out in 10%w/v hydrogen peroxide solution, photolytic (fluorescent light, 10K Lux and UV light, 200watt-hr/m2), thermal (105°C) and humidity (at 90% RH/25°C) according to ICH option 2 of Q1B [11] . These stress samples were analysed by HPLC using proposed method at test concentration to exhibit the ability of the method to separate individual impurities and its degradation impurities at a quantification level. The peak purity test was carried out for the Eletriptan peak by using PDA detector in the stress samples.

Linearity / LOD & LOQ:

The limit of detection (LOD) and limit of quantification (LOQ) for impurities were determined based on the residual standard deviation of a regression line and slope method by injecting a series of dilute solutions with known concentrations. Precision study was also carried out at about LOQ level by injecting impurity-I, impurity-II, impurity-III, impurity-IV and impurity-V calculating % RSD of the areas of each impurity. Linearity solutions were prepared by diluting stock solutions to the required concentrations. The solutions were prepared at six concentration levels from LOQ to around 150% of impurity specification level (i.e 0.15%).

Accuracy: The accuracy study of the impurities were carried out in triplicate at LOQ, 50%,100%, and 150% specification level(0.15%). The sample available for validation work, do not show the presence of impurity-1, impurity-2, impurity-3, impurity-4 and impurity-5. Standard addition and recovery experiments were conducted to determine the accuracy of the related substance method for the quantification of all five impurities in the drug substance sample. The study was performed out by

spiking each impurity at LOQ, 0.07, 0.15, and 0.22% in the sample solution (600µg/mL). The percentages of recoveries for impurity-I, impurity-II, impurity-III, impurity-IV and impurity-V were calculated from amount added and amount found values.

Precision: The method precision of the related substances method was performed by two analyst by injecting six individual preparations of eletriptan hydrobromide with test concentration spiked with 0.15% level of impurities on different days, different columns and on different instruments.

Robustness: To establish the robustness of the method, experimental conditions were deliberately changed, and the resolution between these impurities was evaluated. System suitability solution and sample solution spiked with known related substances at specification level were prepared as per test method, and injected into HPLC at different deliberately varied conditions to evaluate system suitability and method's ability to remain unaffected.

The flow rate was 1.5 mL/min. To study the effect of flow rate on the resolution, flow rate was changed by ±10% from 1.35 to 1.65 mL/min. The effect of pH on resolution of impurities was studied by varying ±0.2 pH units (between 3.8 and 4.2). The effect of the column temperature on resolution was studied 15°C and 25°C instead of 20°C.

The effect of the percent organic strength on resolution was studied by varying % of organic in mobile phase gradient composition by -2% and +2% absolute and also changing % of water in mobile phase B by-2% and +2% absolute by keeping the remaining method conditions constant as mentioned in the method.

Solution stability and mobile phase stability:
The solution stability of Eletriptan hydrobromide and its impurities in the related substances method was carried out by leaving spiked test solutions in tightly capped volumetric flasks at room temperature for 48 h. Contents of impurity-I, impurity-II, impurity-III, impurity-IV and impurity-V were determined for every 5 hours interval and up to 48 hrs. The mobile phase stability was carried out for 48 h by injecting the freshly prepared test solutions for every 5 h interval. Contents of these impurities were evaluated in the test solutions.

RESULTS AND DISCUSSION:

Optimization of HPLC conditions: The important aspect of HPLC method is to separate eletriptan hydrobromide from its five impurities. These Impurities were co eluted using different stationary phases such as C8, C18, phenyl, and cyano columns tried with different mobile phases which containing buffers such as phosphate, sulphate and acetate with different pH(between 2-6) and using organic modifiers like acetonitrile, methanol and tetrahydrofuran in the mobile phase.

Finally the HPLC method was achieved with good separation of eletriptan hydrobromide from impurities using Purospher STAR RP-8e, 250mm x 4.6mm, 5µ column. The mobile phase consists of phosphate buffer with pH 4.0 (Mobile phase A) and solvent mixture of aceteonitrile, water, tetrahydrofuran in the ratio of 70:30:1(v/v/v) (Mobile phase B) with gradient program Time(min)/A(v/v):B(v/v); T0.01/75:25, T30/60:40, T40/35:65, T50/35:65, T52/75:25, T60/75:25. The flow rate of the mobile phase is 1.5 mL/min at 20°C column temperature.

To elute Impurity-6, added 1% tetrahydrofuran in the solvent mixture and by keeping column temperature 20°C only we have achieved better resolution between eletriptan and impurity-III(N-Oxide-1). Hence resolution of 2.0 was kept between eletriptan and impurity- III(N-Oxide-1) in the system suitability criteria. The retention time of eletriptan was 24min and remaining impurities as around 8.2, 21.6, 27.1, 29.1, 30.1, 36.1 & 36.2 min respectively.

The typical HPLC chromatograms of spiked sample, system suitability and diluents are shown in **Fig 2.** The system suitability results are also given in the **Table 1** and the developed HPLC method was found to be specific for eletriptan hydrobromide and its five impurities.

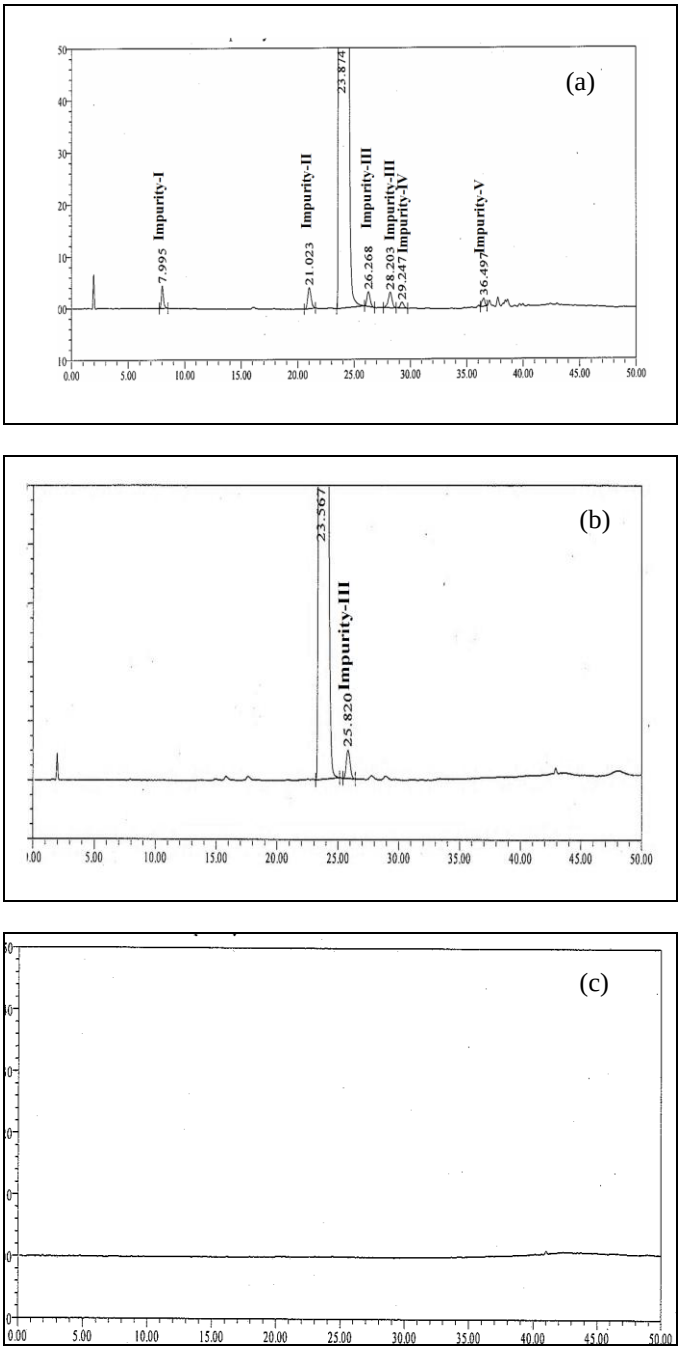


FIG 2: A TYPICAL HPLC CHROMATOGRAMS OF (A) ELETRIPTAN AND ITS IMPURITIES FOR SPECIFICITY (B) SYSTEM SUITABILITY AND (C) DILUENT

Results of forced degradation:

Eletriptan hydrobromide was stable under stress conditions such as acid hydrolysis, basic hydrolysis, thermal stress, humidity stress, and photolytic stress conditions, but considerable degradation of the drug substance was observed under oxidative hydrolysis condition, where one major degradation product at RRT 0.94 was formed under this condition. The typical HPLC chromatograms of forced degradation studies are shown in **Fig 3.**

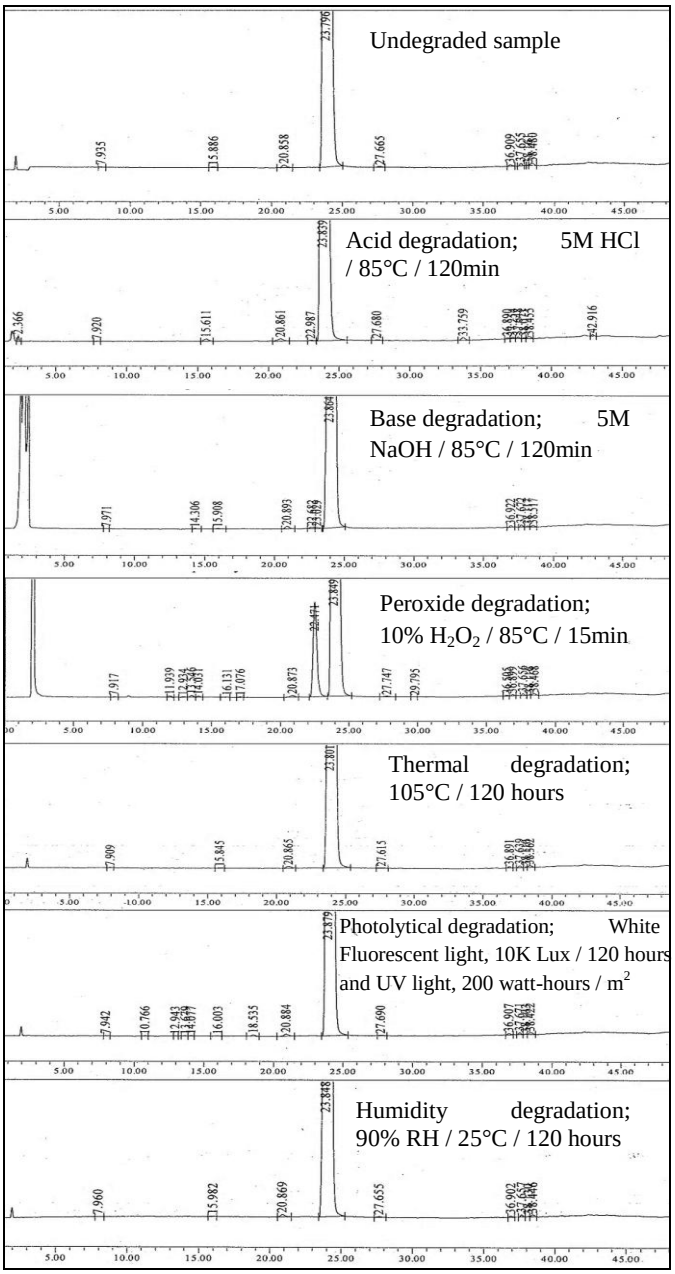


FIG 3: FORCED DEGRADATION HPLC CHROMATOGRAMS

From the peak purity test results obtained in the stressed drug substances sample, the purity threshold is greater than purity angle; this confirms that the Eletriptan peak is homogeneous and pure in all the stress samples analyzed. The assay of Eletriptan hydrobromide is unaffected by the presence of impurities and its degradation products where the mass balance of the undegraded and stressed sample assay value **Table 1** shows the stability-indicating power of the developed HPLC method.

TABLE 1: SPECIFICITY DATA FOR ELETRIPTAN AND ITS IMPURITIES

Compound	RRT	Purity Angle	Purity Threshold	Selectivity	USP Resolution	USP plate count	USP Tailing	K Prime
Impurity-I	0.33	1.188	1.415	--	--	9720	1.33	798.5
Impurity-II	0.88	1.213	1.570	2.6	29.6	24159	1.23	2101.3
Eletriptan	1.00	0.054	0.255	1.1	4.1	13275	1.74	2386.4
Impurity-III [N-Oxide-I]	1.10	1.041	1.818	1.1	3.5	39681	1.21	2625.4
Impurity-III [N-Oxide-II]	1.18	1.054	1.862	1.1	3.4	34940	0.90	2819.3
Impurity-IV	1.23	0.772	1.046	1.0	1.8	45691	1.15	2923.7
Impurity-V	1.53	0.898	1.665	1.2	14.1	82217	0.93	3648.7

TABLE 2: SUMMARY OF LINEARITY / LOD-LOQ EXPERIMENTS

Name	Response Factor	Linearity range(µg/mL)	Correlation Coefficient	LOD (%w/w)	LOQ (%w/w)	LOD (%RSD)	LOQ (%RSD)
Impurity-I	1.06	0.103-1.325	0.9995	0.006	0.017	2.2	1.8
Impurity-II	1.27	0.103-1.342	0.9999	0.006	0.017	5.7	1.1
Eletriptan	1.00	0.087-1.347	0.9999	0.005	0.015	2.8	0.7
Impurity-III [N-Oxide-I]	0.91	0.091-1.360	0.9999	0.005	0.015	6.5	1.2
Impurity-III [N-Oxide-II]	0.91	0.092-1.336	0.9999	0.005	0.015	6.3	0.7
Impurity-IV	2.69	0.255-1.378	0.9999	0.021	0.043	3.8	1.7
Impurity-V	2.49	0.249-1.350	0.9999	0.021	0.042	6.3	0.6

Accuracy: The percentage recovery of impurities in Eletriptan hydrobromide samples were calculated from amount found to amount added values and the recovery data obtained is tabulated in **Table 3.**

TABLE 3: ACCURACY DATA FOR ELETRIPTAN IMPURITIES

Compound	Level (%)	Amount Added	Amount Found	Recovery(%)
Impurity-I	LOQ	0.0173	0.0173	100.0
	50	0.074	0.076	102.3
	100	0.148	0.150	100.9
	150	0.221	0.223	101.1
Impurity-II	LOQ	0.0169	0.0167	98.8
	50	0.075	0.075	100.0
	100	0.150	0.153	101.6
	150	0.225	0.228	101.2
Impurity-III [N-oxide-I]	LOQ	0.0142	0.0140	98.6
	50	0.075	0.076	100.9
	100	0.150	0.151	100.2
	150	0.225	0.230	102.1
Impurity-III [N-oxide-II]	LOQ	0.0143	0.0143	100.0
	50	0.075	0.077	102.2
	100	0.150	0.151	100.5
	150	0.225	0.225	100.0
Impurity-IV	LOQ	0.0430	0.0432	100.5
	50	0.075	0.075	100.0
	100	0.150	0.150	100.0
	150	0.225	0.227	101.0
Impurity-V	LOQ	0.0419	0.0415	99.1
	50	0.075	0.075	100.0
	100	0.150	0.150	100.0
	150	0.225	0.226	100.6

Precision: The areas of each impurity obtained from precision experiment from analyst were subjected to statistical evaluation. The results of analyst I, analyst II and over all statistical data are tabulated in **Table 4**.

TABLE 4: PRECISION DATA

Name	Mean (%w/w)	SD	% RSD	95 % confidence Interval(±)
Impurity-I	0.161	0.002	1.2	0.002
Impurity-II	0.152	0.001	0.7	0.001
Impurity-III [N-Oxide-I]	0.150	0.002	1.3	0.002
Impurity-III [N-Oxide-II]	0.177	0.002	1.1	0.002
Impurity-IV	0.151	0.002	1.3	0.002
Impurity-V	0.150	0.001	0.7	0.001

(Analyst-I) (n=6)

Impurity-I	**0.164**	**0.001**	**0.6**	**0.001**
Impurity-II	0.154	0.002	1.3	0.002
Impurity-III [N-Oxide-I]	0.149	0.002	1.3	0.002
Impurity-III [N-Oxide-II]	0.178	0.001	0.6	0.001
Impurity-IV	0.152	0.002	1.3	0.002
Impurity-V	0.152	0.001	0.7	0.001

(Analyst-II) (n=6)

Impurity-I	**0.163**	**0.002**	**1.31**	**0.001**
Impurity-II	0.153	0.001	0.92	0.001
Impurity-III [N-Oxide-I]	0.150	0.001	0.47	0.000
Impurity-III [N-Oxide-II]	0.178	0.001	0.40	0.000
Impurity-IV	0.152	0.001	0.47	0.000
Impurity-V	0.151	0.001	0.94	0.001

Overall statistical data (n=12)

Robustness: In all the deliberate varied chromatographic conditions (flow rate, column oven temperature, pH and composition of organic solvent), the resolution between eletriptan and its impurities was greater than 2.0 illustrating the robustness of the method. Results are tabulated in the **Table 6a** and **6b**.

TABLE 6A: ROBUSTNESS DATA OF SYSTEM SUITABILITY

Condition	Variation	System Suitability	
		USP Resolution between Eletriptan and Impurity-III [N-oxide-I]	USP Plate count
Acceptance Criteria as per methodology	--	Not less than 2.0	Eletriptan peak is not less than 7000 USP Plate count
As such methodology	-	3.4	12456
Flow	-10%	3.3	13678
	+10%	3.0	11351
Wavelength	-5 nm	3.4	12847
	+5 nm	3.4	12844
% of Organic in MP (Gradient Composition)	-2% absolute	3.2	14727
	+2% absolute	3.0	9925
% of Water in Mobile Phase B	-2% absolute	2.7	9195
	+2% absolute	2.8	10350
Column Oven Temperature	-5°C	3.0	11659
	+5°C	3.3	12540
pH of Buffer	-0.2 unit	3.7	13851
	+0.2 unit	3.0	13890

TABLE 6B: ROBUSTNESS DATA OF SPIKED SAMPLE

Parameter	Variation	RRT						
		Impurity-I	Impurity-II	Eletriptan	Impurity-III [N-oxide –I]	Impurity-III [N-oxide –II]	Impurity -IV	Impurity-V
STP	-	0.34	0.89	1.00	1.10	1.18	1.23	1.53
Flow	-10%	0.35	0.89	1.00	1.10	1.18	1.22	1.46
	+10%	0.33	0.88	1.00	1.11	1.19	1.24	1.59
Wavelength	-5 nm	0.33	0.88	1.00	1.10	1.18	1.23	1.54
	+5 nm	0.33	0.88	1.00	1.10	1.18	1.23	1.54
% of Organic in MP (Gradient Composition)	-2% absolute	0.34	0.89	1.00	1.10	1.17	1.21	1.39
	+2% absolute	0.34	0.89	1.00	1.11	1.20	1.24	1.68
% of Water in Mobile Phase B	-2% absolute	0.33	0.88	1.00	1.09	1.17	1.22	1.46
	+2% absolute	0.34	0.88	1.00	1.09	1.17	1.21	1.51
Column Oven Temperature	-5°C	0.34	0.88	1.00	1.10	1.18	1.22	1.48
	+5°C	0.34	0.90	1.00	1.10	1.18	1.24	1.61
pH of Buffer	-0.2 unit	0.33	0.88	1.00	1.10	1.19	1.23	1.52
	+0.2 unit	0.33	0.88	1.00	1.09	1.17	1.23	1.52

Solution stability and mobile phase stability:
The % RSD of has no significant changes when we were observed in the content of impurity levels during solution stability and mobile phase stability experiments when performed using the related substance method. The solution stability and mobile phase stability experiment data confirms that the sample solutions and mobile phases used during assay and the related substance determination were stable for at least 48 h.

Application of the developed HPLC method to stability samples and quality monitoring of Eletriptan hydrobromide:
Accelerated and long-term stability studies are carried out to establish retest period or a shelf life of drug product [12]. Eletriptan hydrobromide samples stored at long-term condition (temp: 25 C ± 2 C, relative humidity 60 ± 5%) and accelerated condition (temp:40 C ± 2C relative humidity 75 ± 5%) were analyzed by using the developed HPLC method for a period of 6 months at different intervals.

Also, the quality of Eletriptan hydrobromide was monitored during the production of three batches by using the developed HPLC method. The results clearly indicated that the drug was stable under long term and accelerated conditions, and there were no interference of the impurities for Eletriptan hydrobromide, which demonstrates that developed HPLC method was stability- indicating and well applied for drug stability studies as well as for quality monitoring of Eletriptan hydrobromide drug substance.

CONCLUSION: In this paper a simple validated and well defined specific stability indicating HPLC method for the determination of Eletriptan hydrobromide as well as its related substances was described, and the behaviour of Eletriptan hydrobromide drug substances under various stress conditions was studied and presented. All the degradation products and process impurities were well separated from the main elute, which demonstrates that the method is stability indicating. The information presented here in could be very useful for quality monitoring of bulk drug samples, and also employed to monitor the quality of the drug substances during stability studies.

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REFERENCES:

1. http://www.drugs.com/monograph/eletriptan-hydrobromid e.html
2. Evans DC, Connor OD, Lake BG, Evers R, Allen C and Hargreaves R: Eletriptan metabolism by human hepatic CYP450 enzymes and transport by human P-glycoprotein. Drug Metab Dispos 2003; 31: 861-869.
3. http://www.pfizer.ca/en/our_products/products/monograph/139
4. Zecevic M, Jocic B, Kustrin KSA and Zivanovic L: Validation of an HPLC method for the simultaneous determination of eletriptan and UK 120.413. J Serb Chem Soc 2006; 71: 195-1205.doi: 10.2298/JSC0611195Z.
5. Suneetha D and Lakshmana Rao: RP-HPLC Method for the estimation of Eletriptan in pharmaceutical dosage Forms. IJCEPR 2010; 1: 95-99.
6. Balaji N, Sivaraman VR and Neeraja P: A validated UPLC method for the determination of process-related impurities in antimigraine bulk drug. IOSR Journal of Applied Chemistry 2013; 3: 20-28.
7. Bagary RIEl, Mohammed NG and Nasr HA: Fluorimetric and colorimetric methods for the determination of some antimigraine drugs. J Chem Pharm Res 2011; 3: 304-314.
8. Armagan Onal: Spectrophotometric and spectrofluorimetric determination of some drugs containing secondary amino group in bulk drug and dosage forms via derivatization with 7-chloro-4-nitrobenzofurazon. Quim Nova 2011; 34: 677-682.
9. Bagary RIEl, Mohammed NG and Nasr HA: Two Chromatographic methods for the determination of some antimigraine. Drugs. Anal Chem Insights 2012; 7:13–21. doi: 10.4137/ACI.S8864
10. ICH Harmonised tripartite guideline, Validation of analytical procedures: Text and Methodology Q2 (R1) 2005.
11. ICH Harmonised tripartite guideline, Stability testing: Photostability testing of new drug substances and products Q1B 1996.
12. ICH Harmonised tripartite guideline, Stability testing of new drug substances and products Q1A (R2) 2003.

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