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# Method Develop and Validation of Eletriptan Hydrobromide Pharmaceutical Dosage Form By Rp-Hplc

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**Abstract**
A reverse phase high performance liquid chromatographic method has been described for the estimation of Eletriptan Hydrobromide in its pharmaceutical dosage forms using symmetry $C_{18}$ (4.6×100nm, 3.5µm) column. In isocratic mode using phosphate buffer: Acetonitrile ratio of 60:40 v/v. The detection was carried out using UV detector at 221 nm. The linearity of Eletriptan Hydrobromide was found to be in the concentration range of 10 to 50 µg/ ml. The flow rate was 0.9 ml/min and the run time was 6 min. The Eletriptan Hydrobromide retention time was observed to be 2.29min .The developed method was validated with respect to linearity, precision, accuracy and specificity as per the International Conference on Harmonisation (ICH) guidelines. The mean recoveries were found to be within the limits. The developed method was simple, fast, accurate and precise and has been successfully applied for the analysis of Eletriptan Hydrobromide in bulk sample and in pharmaceutical dosage forms.
**Keywords:** Eletriptan Hydrobromide, Phosphate Buffer, Acetonitrile, Retention Time, linearity

## I. INTRODUCTION

Eletriptan, 3-((*R*)-1-methyl-2-pyrrolidinyl) Methyl)-5-_2-(phenylsulfonyl) ethyl-indole hydrobromide (Fig. 1), is a new orally active 5-HT 1B/1D agonist, recently approved by the Food and Drug Administration for the acute treatment of migraine headache.

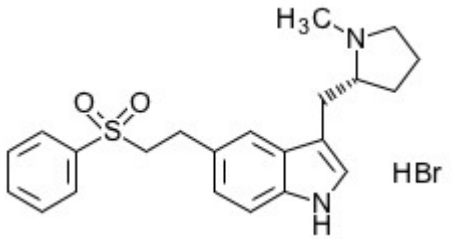


**Figure 1 Eletriptan Hydrobromide**

Eletriptan Hydrobromide is believed to reduce swelling of the blood vessels surrounding the brain. This swelling is associated with the head pain of a migraine attack. Eletriptan Hydrobromide blocks the release of substance from nerve endings that cause more pain and other symptoms like nausea, and sensitivity to light and sound. It is thought that these actions contribute to relief of symptoms by Eletriptan Hydrobromide. A simple and accurate reverse phase liquid chromatographic and UV-VIS methods are developed for the determination (1, 8) of Eletriptan hydrobromide.

Pharmaceutical analysis includes both qualitative and quantitative analysis of drugs and pharmaceutical substances starts from bulk drugs to the finished dosage forms. Most frequently used methods for quality analysis are UV spectroscopy, FTIR and liquid chromatography and Mass spectroscopy etc. Among them High performance liquid chromatography is basically a highly improved form of column chromatography. Instead of a solvent being allowed to drip through a column under gravity, it is forced through under high pressures of up to 400 atmospheres (2,4). That makes it much faster. It also allows you to use a very much smaller particle size for the column packing material which gives a much greater surface area for interactions between the stationary phase and the molecules flowing past it. The chemical interaction of the stationary phase and the sample within the mobile phase determines the degree of migration and separation of the components contained in the sample is the basic principle for High performance liquid chromatography (HPCL) (3,9). RP-HPLC operates on the principle of hydrophobic interactions, which originates from the high symmetry in the dipolar water structure and plays the most important role in all processes in life science. RP-HPLC allows the measurement of these interactive forces. The binding of the analyte to the stationary phase is proportional to the contact surface area around the non-polar segment of the analyte molecule upon association with the ligand on the stationary phase. The validation criteria were given in Table -1.

**Table-1: Criteria for Validation of the Method**

| CHARACTERISTICS | ACCEPTABLE RANGE |
|---|---|
| Accuracy | Recovery (98-102%) |
| Precision, | RSD < 2% |
| Intermediate precision | RSD < 2% |
| Specificity | No |

| | Interference |
|---|---|
| LOD | S/N > 2 or 3 |
| LOQ | S/N > 10 |
| Linearity | Correlation Coefficient( r)>0.99 |
| Range | 80-120% |
| Stability | >24h or >12h |

However, the best of our knowledge there is no available analytical method for Eletriptan hydrobromide, for its elution within a short duration. The aim of the present work is to develop a specific, precise, accurate and rapid method to elute the Eletriptan hydrobromide in short span of time.

## II. MATERIAL AND METHODS

The Chemicals/ Reagents, Solvents and instruments used are given in below table- 2 and 3

**Table-2: Shows Chemicals and Reagents**

| S. No. | Chemicals/standards and reagents | Grade | Make |
|---|---|---|---|
| 1 | Potassium dihydrogen phosphate | HPLC | Fisher |
| 2 | Ortho phosphoric acid | HPLC | Fisher |
| 3 | HPLC Grade Methanol | HPLC | Merck |
| 4 | HPLC Grade Acetonitrile | HPLC | Merck |
| 5 | Double Distilled Water | HPLC | Merck |
| 6 | Eletriptan Hydrobromide | N/A | |

Eletriptan Hydrobromide is a serotonin agonist, specifically, it is a selective 5-hydroxytryptamine 1B/1D(5-HT1B) receptor agonist. Eletriptan Hydrobromide binds with high affinity to the 5-HT1B,1D,1F receptors. It has a modest affinity to the 5-HT1A,1E,3B,7 receptors(12)

**Physical Properties:**

Mol.Mass : 382.52 g/mol
Melting Point : 169-171°C
PKa : Strongest acid -17.11
Strongest base - 8.37
Water Solubility : Soluble

**Table- 3: Shows Instruments and Equipments**

| S.No. | Instruments and Equipments | Software | Model | Company |
|---|---|---|---|---|
| 1 | HPLC | N 2000 chromato graphic system | Waters 515pump, Detector 2487 | WATERS |
| 2 | UV-Spectrophotometer | UV Analyst | UV-2310 | TECHCOMP |
| 3 | Weighing Balance | N/A | XEX 200 | SHIMADZU |
| 4 | Sonicator | N/A | SE60US | ENERTECH |
| 5 | pH Meter | N/A | AD102U | ADWA |

## III. RESULTS AND DISCUSSION:

UV spectrum was recorded for Eletriptan Hydrobromide individually and the Lambda max of Eletriptan Hydrobromide was found to be 215 nm. UV-VIS spectrogram of Eletriptan Hydrobromide has shown in fig- 2. It was found that Eletriptan Hydrobromide can effectively be analyzed by using the RP- HPLC method (4, 11).

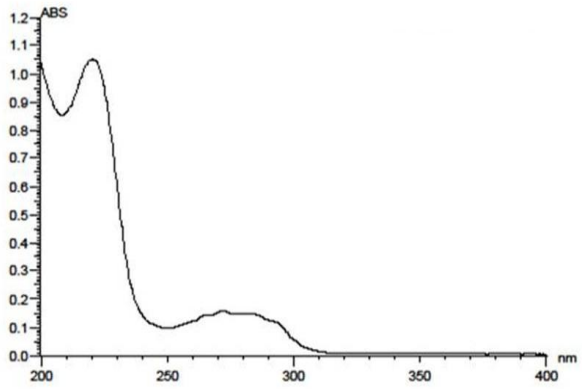


**Fig 2: UV-VIS spectrum and accuracy assessment of Eletriptan hydrobromide**

**Table-4: Accuracy Observation of Eletriptan Hydrobromide**

| % Concentration (at specification Level) | Area | Amount Added (mcg) | Amount Found (mcg) | % Recovery | Mean Recovery |
|---|---|---|---|---|---|
| 50 % | 1982240 | 15.0 | 14.98 | 99.89 | 101.96 |
| 100 % | 2594119 | 30.0 | 30.59 | 101.96 | |
| 150 % | 3269320 | 45.0 | 45.86 | 101.91 | |

The accuracy studies were shown as % recovery for Eletriptan Hydrobromide at 50 %, 100 % and 150 %( Table-4) the limits of % recovered should be in the range of 98-102 %. The results obtained for Eletriptan Hydrobromide were found to be within the limits. Hence the method was found to be accurate (fig-3)

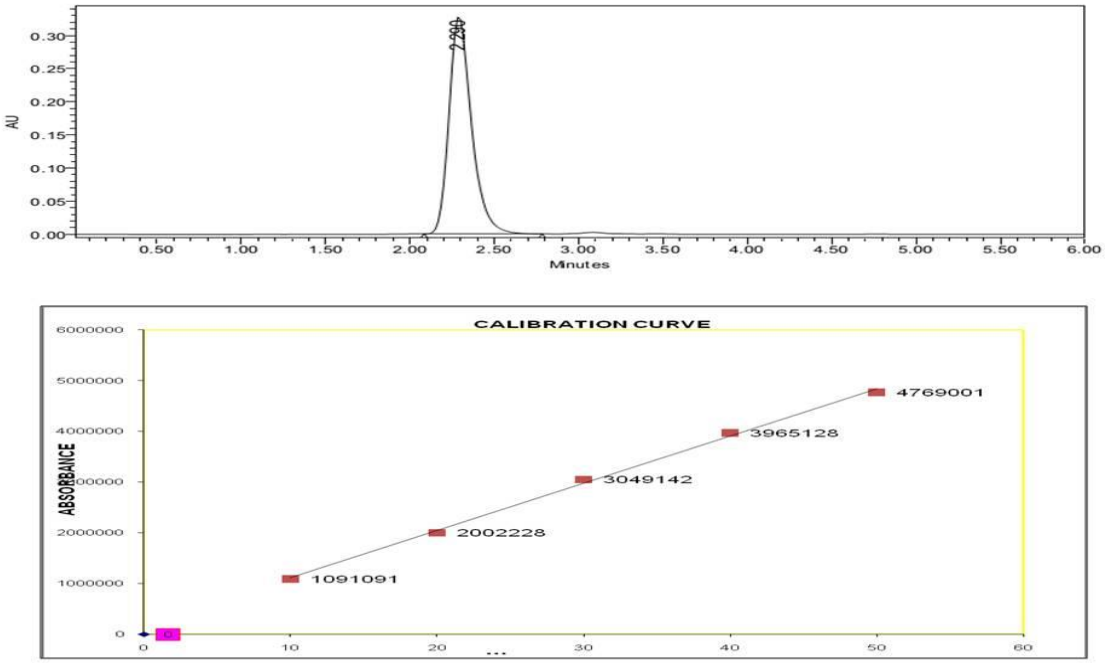


**Fig 3: Precision and linearity of the Eletriptan at deferent dosages**

**Table-5: Observation of System Precision**

| INJECTION | ELETRIPTAN HYDROBROMIDE AREA |
|---|---|
| Injection1 | 2977138 |
| Injection2 | 2917756 |
| Injection3 | 2861139 |
| Injection4 | 2922541 |
| Injection5 | 2908272 |
| Average | 2917369 |
| Standard Deviation | 41363.63 |
| % RSD | 1.41784 |

The precision of an analytical procedure expresses the closeness of agreement among a series of measurements obtained from multiple samplings of the same homogenous sample under prescribed conditions. In this study 5 replicate injections of Eletriptan Hydrobromide formulation (method precision) was performed %RSD was determined for peak areas (Table-5). The acceptance limit should be not more than 2 % and the results were obtained for standard samples (method precision) were found to be within the acceptance limits (6).

**Table-6: Observation of Intermediate System Precision**

| Injection | ELETRIPTAN HYDROBROMIDE Area |
|---|---|
| Injection1 | 3045134 |
| Injection2 | 3042317 |
| Injection3 | 3041284 |
| Injection4 | 3047977 |
| Injection5 | 3056220 |
| Mean | 3046586.4 |
| Standard Deviation | 5983.15772 |
| % RSD | 0.196388907 |

For Intermediate precision studies 5 replicate injections (Table-6) formulation (method id precision) was performed. % RSD was determined for peak areas of sample of ELETRIPTAN HYDROBROMIDE. The acceptance limit are should be not more than 2 % and the results were obtained for sample (method ID precision)were found to be within the acceptance limits.

The linearity of an analytical procedure is its ability (within a given range) to obtain test results, which are directly proportional to the concentration of the analyte in the sample represented in fig-3 (10). The linearity range was found to be 10-50 µg/ml for Eletriptan Hydrobromide. Calibration curve was plotted and correlation co-efficient for all the drugs are found to be 0.999. Hence the results obtained were within the acceptable limits.

**Table-7: Flow rate observation of Eletriptan Hydrobromide**

| S.No | Flow Rate (ml/min) | ystem Suitability Results | |
|---|---|---|---|
| | | USP Plate Count | SP Tailing |
| 1 | 0.8 | 2516 | 1.3 |
| 2 | 0.9 | 2549 | 3 |
| 3 | 1.0 | 2335 | 1.3 |

***** Results for actual flow (ml/min) have been considered from Assay standard

**Table-8: Observation of System Suitability Parameters**

| S. No | Parameter | ELETRIPTAN HYDROBROMIDE |
|---|---|---|
| 1 | Retention time | 2.3 |
| 2 | Theoretical plates | 2549.0 |
| 3 | Tailing factor | 1.3 |
| 4 | Area | 3040909 |

The system suitability Parameters were found to be within the specified limits (Table-8) for the proposed method.

**Table-9: Summarized RP-HPLC Method for Eletriptan Hydrobromide**

| S.No | Parameter | Acceptance criteria | Results |
|---|---|---|---|
| 1 | System suitability | Theoretical Plates-NLT2000 | 2549 |
| | | Tailing factor-NMT 2 | 1.3 |
| | | Resolution-NLT 2 | 0.0 |
| 2 | Precision | % RSD | 1.41 |
| 3 | ID Precision | % RSD | 0.19 |
| 4 | Linearity | Correlation coefficient NLT 0.999 | 0.9990 |
| 5 | Accuracy | Percentage Recovery 98-102% | 101.96 |
| 6 | LOD | 0.19ug/ml | |
| 7 | LOQ | 0.64ug/ml | |

The limit of detection (LOD) represents the concentration of analyte. The limit of detection for the Eletriptan hydrobromide was found to be 0.19 µg $ml^{-1}$ for 10 µl (Table-9) of injection volume. The LOQ represents the concentration of analyte that would yield a signal-to-noise ratio of 10 (fig-3). The limit of quantitation for the *S*-isomer was found to be 0.64 µg $ml^{-1}$ for the 10 µl of injection volume (5).

The ruggedness of a method was defined as degree of reproducibility of results obtained by analysis of the same sample under a variety of normal test conditions such as different laboratories, different analysts, different instruments and different days(7).

The robustness of an analytical procedure is measured by its capability to remain unaffected through small, but deliberate, variations in method parameters and provide an indication of its reliability during normal usage. In the varied chromatographic conditions like flow rate was found to be >2.0 illustrating the robustness of the method. The results are summarized on evaluation of the above results, it can be concluded that the variation in flow rate affected the method significantly (table-7). Hence it indicates that the method is robust even by change in the flow rate ±10 %.

The method is robust only in less flow condition.

## IV. CONCLUSION

- The evaluation of obtained values suggests that the proposed HPLC methods provide simple, precise, rapid and robust quantitative analytical method for estimation of Eletriptan HydroBromide in pharmaceutical dosage form.
- The mobile phase is simple to prepare and economical.
- As I validated method as per ICH guidelines and correlating obtained values with the standard values, satisfactory results were obtained.
- Hence, the method can be easily and conveniently adopted for routine estimation of Eletriptan HydroBromide in pharmaceutical dosage form.

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