VALIDATION OF DEVELOPED METHOD FOR ZOLMITRIPTAN TABLETS IN PHARMACEUTICAL DOSAGE FORM BY RP-HPLC

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ABSTRACT
Zolmitriptan acts as Anti-inflammatory Agents, Anti-migraine Agents, Selective Serotonin Agonists and Vasoconstrictor Agents. A new RP-HPLC method was developed for the determination of Zolmitriptan ((4R)-4-[3-(2-dimethylaminoethyl)-1H-indol-5-yl] methyl]-1, 3- oxazolidin-2-one) in tablet dosage form. The HPLC method was then validated to indicate that the analytical procedure used is suitable for intended use by using various parameters like specificity, linearity, and precision, and accuracy, stability in analytical solution, system suitability and filter interference. A new, specific stability indicating method was developed. This Validation describes the procedure for assay of Zolmitriptan (MF: C₁₆H₂₁N₃O₂) tablets 5 mg by HPLC as per ICH Guidelines and can be applicable for the analysis of commercial dosage forms. X-TerraRP-18, 250x4.6mm,5µ column, injection volume20 µl, Column temperature 30°C, run time 8 minutes with a hydrophilic linkage between silica particles and hydrophobic alkyl chains. Using isocratic elution with UV detection at 225 nm.

Keywords: Zolmitriptan, RP-HPLC, ICH.

1. INTRODUCTION
Zolmitriptan binds with high affinity to human 5-HT₁B and 5-HT₁D receptors leading to cranial blood vessel constriction. Current theories proposed to explain the etiology of migraine headache suggest that symptoms are due to local cranial vasodilatation and/or to the release of sensory neuropeptides (vasoactive intestinal peptide, substance P and calcitonin gene-related peptide) through nerve endings in the trigeminal system. The therapeutic activity of zolmitriptan for the treatment of migraine headache can most likely be attributed to the agonist effects at the 5HT₁B/₁D receptors on intracranial blood vessels (including the arterio-

<table>
<thead>
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<th>S. No.</th>
<th>Name of Instrument</th>
<th>Model</th>
<th>Make</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Semi micro balance</td>
<td>CPA225D</td>
<td>Sartorius</td>
</tr>
</tbody>
</table>

Venous anastomoses) and sensory nerves of the trigeminal system which result in cranial vessel constriction and inhibition of pro-inflammatory neuropeptide release.

2. MATERIALS
Table No: 1 list of materials
Reagents and chemicals:

Table No: 2 list of Reagents and chemicals

<table>
<thead>
<tr>
<th>No.</th>
<th>Chemicals/Reagents</th>
<th>Make/Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Acetonitrile</td>
<td>Merck, (HPLC-Grade)</td>
</tr>
<tr>
<td></td>
<td>Potassium dihydrogen orthophosphate</td>
<td>Merck (GR-Grade)</td>
</tr>
<tr>
<td>2</td>
<td>Sodium Hydroxide</td>
<td>Merck, (GR-Grade)</td>
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</tbody>
</table>

Working/reference standards – Zolmitriptan

Filter  
0.45μm GHP membrane filter (Manufactured by PALL) and 0.45μm PVDF membrane filter (Manufactured by PALL).

Test sample  
Zolmitriptan tablets 5 mg and Zolmitriptan tablets Placebo.

3. METHODOLOGY

Method Development by RP-HPLC

Preparation of buffer solution (Mobile Phase-A)

Weighed accurately about 6.85358g of sodium dihydrogen orthophosphate and 1.75023g of disodium hydrogen phosphate dihydrate and transferred into 5 liter bottle. Added 5 liter water and mixed well using magnetic stir bar until the material dissolved completely. Mixed well, checked the pH and adjusted to 7.8 ±0.05 with triethylamine. Filter the solution through 0.45 μm nylon membrane filter and degassed by sonicating for 5 minutes.

Mobile phase B  
Acetonitrile.

Preparation of Diluent

Transferred 750ml of buffer and 250 ml of Acetonitrile into 1 liter bottle, Mixed well and degassed by sonicating for 5 minutes.
Standard preparation

Weighed accurately about 52.54 mg of Zolmitriptan working standard and transferred into a 100 ml volumetric flask. Added about 50 ml of diluent to dissolve by sonicating for 5 minutes and completed to volume with diluent.

Sample Preparation for Assay

Weighed accurately 10 tablets and transferred to mortar, and crushed the sample and weigh equivalent to 80 mg of Zolmitriptan (3988.38mg) and transferred to 100 ml volumetric flask. To this added about 50 ml of diluents and sonicated for 20 minutes. Completed to volume with diluent and filtered through 0.45µ GHP filter. Further pipetted 3ml to 25ml and completed to volume with diluent.

Trial No. 1

Trial No. 2

Trial No. 3

HPLC chromatogram for optimized chromatographic parameters

Figure: 5 HPLC chromatogram of trial 1

Figure: 6 HPLC chromatogram of trial 2

Figure: 7 HPLC chromatogram of trial 3

Figure: 9 HPLC Chromatogram of blank

Figure: 10 HPLC chromatogram of standard Zolmitriptan
Figure: 11 HPLC chromatogram of sample drug of Zolmitriptan

Figure: 12 HPLC chromatogram of Zolmitriptan linearity 25%

Figure: 13 HPLC Chromatogram of Zolmitriptan linearity 50%

Figure: 14 HPLC chromatogram of Zolmitriptan linearity 75%

Figure: 15 HPLC chromatogram of Zolmitriptan linearity 100%

Figure: 16 HPLC chromatogram of Zolmitriptan linearity 125%

Figure: 17 HPLC chromatogram Zolmitriptan 150%
4. **SUMMARY**

A HPLC method for Zolmitriptan was developed and validated in tablet dosage form as per ICH Guidelines. Agilent 1200 series with DAD Detector and Waters X-terra (250 × 4.6 mm, 5 µl) column, injection of 10 µl is injected and eluted with the mobile phase of sodium dihydrogen orthophosphate buffer with 0.2M of 7.8 pH and acetonitrile in the ratio 80:20v/v, which was pumped at a flow rate of 1.0 ml at 225 nm. The peak of Zolmitriptan was found well separated at 4.2 min. The analytical method validation of Zolmitriptan by RP HPLC method was found to be satisfactory and could be used for the routine pharmaceutical analysis of Zolmitriptan.

5. **CONCLUSION**

The proposed RP-HPLC method is suitable for the estimation of Zolmitriptan in formulation. All the validation parameters for Zolmitriptan meet the criteria as per ICH guidelines. The analytical method was found to be simple, sensitive, accurate and precise. The developed methods may be recommended for routine and QC analysis of the investigated drug to provide reproducible quantitative analysis for the determination of Zolmitriptan in tablet formulation.

**BIBLIOGRAPHY**


