A Rapid Determination of Cinnarizine in Bulk and Pharmaceutical Dosage Form by LC

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Received 14 October 2009; Accepted 7 December 2009

Abstract: A simple, selective, rapid and precise reverse phase high pressure liquid chromatographic method has been developed for the estimation of cinnarizine from pharmaceutical formulation. The method was developed using MICRA-NPS C18 (length×OD×ID =33×8.0×6.0 mm, 1.5 µm) column with a mobile phase consisting of acetonitrile, triethylamine buffer (adjusted to pH 4.5 with 10% w/v potassium hydroxide) and tetrahydrofuran in the ratio 30:66:4 respectively, at a flow rate of 0.5 mL/min. Wavelength was fixed at 253 nm. The developed method was validated for linearity, accuracy, precision, limit of detection and limit of quantitation. The proposed method can be used for the routine estimation of cinnarizine in pharmaceutical dosage form.

Keywords: Column liquid chromatography, Cinnarizine, Meniere’s disease.

Introduction

Cinnarizine (CINN), chemically designated as 1-(diphenylmethyl)-4-(3-phenyl-2-propenyl)piperazine (Figure 1), widely used for prophylaxis and treatment of vertigo associated with Meniere’s disease. CINN exerts its antivertigo effects primarily on the peripheral vestibular system through inhibition of calcium influx1,2. CINN is official in B.P. indicates non-aqueous titrimetric method3. Literature survey states the availability of various methods for quantification of CINN in pharmaceutical preparations and biological materials like spectrophotometry, polarography, potentiometry, voltammetry, GC, HPTLC and HPLC. The simultaneous determination of CINN and domperidone by spectrophotometry has also been reported. The reported HPLC method, requires the long run due to higher retention time (as high as 22 min), whereas other analysis methods are not suitable for routine analysis4-9. Therefore, in the present investigation a new, simple, accurate, sensitive and precise RP-HPLC method has been developed for the determination of CINN in bulk and marketed formulation for routine analysis.
A Rapid Determination of Cinnarizine

**Experimental**

CINN was assayed by reverse phase HPLC method. The HPLC system (DIONEX, Germering, Germany) consisting of Chromelone acquisition software (version 6.70) equipped with P 680 HPLC pump, ASI-100 automated sample injector and UVD 170 UV detector. The HPLC column used was MICRA-NPS RP18 (length×OD×ID = 33×8.0×6.0 mm, 1.5 µm). Isocratic elution was performed using mobile phase, consisting acetonitrile, triethylamine buffer (adjusted to pH 4.5 with 10% w/v potassium hydroxide) and tetrahydrofuran in the ratio 30:66:4 respectively, at flow rate of 0.5 mL/min. The volume of sample injected was 05 µL. The detection wavelength for CINN was set at 253 nm; responses of peak areas were recorded and integrated using software.

*Preparation of standard stock solutions and calibration curve*

Standard stock solution of a concentration of 200 µg mL\(^{-1}\) of CINN was prepared using mixture of ethanol and acetate buffer (pH 5.5) in 1:1 proportion (solution A). From the standard stock solution, standard solutions in the range of 20-100 µg mL\(^{-1}\) were prepared. An aliquot (05 µL) was injected and each chromatogram was recorded. A representative chromatogram is given in Figure 2. Calibration curves were obtained by plotting the response factor versus the concentration.

![Figure 2. Representative chromatogram of cinnarizine.](image-url)
**Procedure for analysis of marketed formulation**

Twenty tablets (trade name: Stugeron FC TAB), each containing 75 mg of CINN were weighed and finely powdered. A quantity of powder equivalent to 75 mg was weighed and transferred to a 50 mL volumetric flask containing about 40 mL solution A, ultrasonicated for 10 min and then the volume was made up to 50 mL with solution A. The solution was filtered using whatmann filter paper No.41. From the filtrate appropriate dilutions were made to obtain concentrations in the range of 20-100 µg mL$^{-1}$ of CINN. Before injecting onto the column, all the standard samples were filtered through 0.22 µm Nylon filter (Millipore), using a syringe filter (Tarsons) mounted on the Luer Lok syringe (Becton Dickinson). The tablet sample solution was injected and the chromatogram was recorded. The peak area ratio of drug was calculated and the amount of each drug present per tablet was estimated from the calibration curve.

**Method validation**

As per the ICH guidelines, method validation parameters checked were linearity, accuracy, precision, limit of detection, limit of quantitation and robustness\textsuperscript{10-11}.

**Linearity and precision**

The linearity of the method was determined at five concentration levels ranging from 20 to 100 µg mL$^{-1}$.

**Accuracy and precision**

The accuracy of the method was determined by recovery experiments. The recovery study was carried out by the standard addition method at three levels of 80, 100 and 120%. Each solution was injected in triplicate and the percentage recovery was calculated. Recovery was within the range of 100 ± 2% which indicates accuracy of the method. The precision of the method was demonstrated by intra-day and inter-day variation studies. In the intra-day studies, three repeated measurements of standard and sample solutions were made in a day and percentage relative standard deviation (RSD) were calculated. In the inter-day variation studies, three repeated measurements of standard and sample solutions were made on three consecutive days and % RSD were calculated. The value of not more than 1.5% indicates that the developed method is precise (Table 2). The Limit of Detection and Limit of Quantification were found to be 0.0592, 0.1794 µg mL$^{-1}$ respectively.

**Robustness**

A deliberate change in the mobile phase composition was made and the changes in the areas of peaks of interest were noted. The peak areas were not significantly affected and hence, the method was found to be robust.

**Results and Discussion**

For the RP-HPLC method, chromatographic conditions were optimized to achieve the best resolution and peak shape for CINN. Different mobile phases containing acetonitrile, methanol, triethylamine buffer and tetrahydrofuran were examined and the mobile phase containing acetonitrile, triethylamine buffer and tetrahydrofuran in the ratio 30:66:4 respectively, was selected as optimal for obtaining well-resolved peaks with acceptable system suitability parameters (theoretical plates, resolution factor and asymmetry). The optimum wavelength for detection and quantitation was 253 nm, at which the best detector response was obtained. The method was found to be linear in the concentration range of
20-100 µg mL^-1 (Table 1). It was also found to be accurate, precise and robust with acceptable values of LOD and LOQ. Table 2 & 3 shows assay results, precision studies, recovery analysis for the developed method.

### Table 1. Validation parameters for reverse phase HPLC method.

<table>
<thead>
<tr>
<th>Performance Parameters</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wavelength, nm</td>
<td>253</td>
</tr>
<tr>
<td>Range</td>
<td>20-100</td>
</tr>
<tr>
<td>Correlation coefficient (r) (^a)</td>
<td>0.999</td>
</tr>
<tr>
<td>Retention time, min</td>
<td>1.27</td>
</tr>
<tr>
<td>Asymmetric factor</td>
<td>1.39</td>
</tr>
<tr>
<td>Detection limit, µg/ mL</td>
<td>0.0592</td>
</tr>
<tr>
<td>Quantitation limit, µg/ mL</td>
<td>0.1794</td>
</tr>
<tr>
<td>No. of data points</td>
<td>5</td>
</tr>
</tbody>
</table>

\(^a\) With respect to \(y = mx + c\), where \(y\) is the absorbance and \(x\) is the concentration (µg/ mL).

### Table 2. Assay results and precision studies.

<table>
<thead>
<tr>
<th>Sample</th>
<th>Labelled amount, mg/ tablet</th>
<th>Amount found in mg %, label claim ±SD(^*)</th>
<th>Precision**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cinnarizine Tablets (Stugeron FC)</td>
<td>75</td>
<td>74.12</td>
<td>98.70 ± 0.275</td>
</tr>
<tr>
<td>Interday</td>
<td>0.0027</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intraday</td>
<td>0.0041</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\(^*\)Average of three determinations, \(^**\)SD of three determinations

### Table 3. Recovery study.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Label claim mg/tab</th>
<th>Estimated amount</th>
<th>Spike level, %</th>
<th>Amount of drug added, mg</th>
<th>Amount of drug recovered, mg</th>
<th>Percentage recovery ±SD(^*)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cinnarizine Tab</td>
<td>75</td>
<td>74.12</td>
<td>80</td>
<td>4</td>
<td>4.03</td>
<td>101.05 ±0.2706</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>100</td>
<td>5</td>
<td>4.98</td>
<td>99.59 ±0.4150</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>120</td>
<td>6</td>
<td>6.01</td>
<td>100.53±0.5791</td>
</tr>
</tbody>
</table>

\(^*\)Mean of three determinations

### Conclusion

The validated RP-HPLC method employed here proved to be simple, fast, accurate, precise and sensitive and thus, can be used for the routine estimation of cinnarizine in pharmaceutical dosage form.

### Acknowledgments

The authors are thankful to Unichem (Mumbai, India) for providing cinnarizine as a gift sample. The authors are also grateful to Principal, Government College of Pharmacy, Aurangabad, for providing necessary facilities for the research work.

### References

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