RP-HPLC Method for the Estimation of Montelukast Sodium in Pharmaceutical Dosage Forms

Shanmukha Kumar J.V. 1*, Ramachandran D. 2 and Vijaya Saradhi S. 3
1 Dept. of Chemistry and 2 Dept. of Biotechnology, College of Engineering, K.L.University, Vaddeswaram – 522 502, Guntur, A.P, India.
3 Dept. of Chemistry, Acharya Nagarjuna University, Nuzvid Campus, Nuzvid, Krishna District, A.P, India.
*For Correspondence - shanmuk_fed@klce.ac.in

Abstract
A reverse phase high pressure liquid chromatographic method (HPLC) has been described for the estimation of Montelukast Sodium in its pharmaceutical formulations using an inertsil ODS C-18, 5 µm column having 250x4.6 mm I.D. in gradient mode, with mobile phase A, containing 0.02 M sodium phosphate buffer: methanol (85:15) and mobile phase B, containing acetonitrile: methanol (85:15), at different time intervals. The flow rate was 1.0 ml/min and effluent was monitored at 218 nm and the linearity was found to be in the range of 0.1 to 10 µg/ml. The method is simple, precise, specific, less time consuming and accurate for the estimation of montelukast Sodium in Pharmaceutical dosage forms.

Key Words : HPLC, Montelukast Sodium, Pharmaceutical Dosage Forms, Retention time, Linearity

Introduction
Montelukast Sodium (1,2) is [R-(E)]=1-[[1-[3-[2-(7-chloro-2quinolinyl) ethenyl] phenyl]- 3-[2-(1-hydroxy-1-methylethyl)phenyl] propyl] thio]methyl] cyclopropane acetic acid, sodium salt (mono), a leukotriene receptor antagonist used as an alternative to anti-inflammatory medications in the management and chronic treatment of asthma and exercise-induced bronchospasm (EIB) that is marketed under trade names such as Singulair® and Montair. Only a very few analytical methods have been reported for its estimation in pharmaceutical dosage forms by HPLC (3, 4, 6, 9, 11) Spectrofluorimetry (5) Electrophoresis (10), UV Spectrophotometer (7, 8) and LC-ESI-MS (12). In the present study a sensitive, specific, precise and accurate HPLC method has been developed for the estimation of Motelukast Sodium in pharmaceutical dosage forms. The structure of the drug with reactive functional groups is given below (Figure 1).

![Structure of Montelukast Sodium with Reactive functional groups](image1.png)

Fig. 1. Structure of Montelukast Sodium with Reactive functional groups

Materials and Methods
Experimental Montelukast Sodium was a gift sample from local pharmaceutical industry. Acetonitrile, Methanol and triple distilled water (TD water) used were of HPLC grade (Qualigens). All other reagents (Sodium phosphate buffer) used in the study were of AR quality (Qualigens).
A gradient high pressure liquid chromatograph (Shimadzu HPLC class VP series) with two LC-20 AT VP pumps, variable wavelength programmable UV–Visible detector SPD-20 A VP ,SCL-20A VP system controller (Shimadzu) and a reverse phase C-8 column (250x4.6 mm, 5µ) was used for estimation. The HPLC system was equipped with the software “class VP series version 5.03 (Shimadzu)"

**Chromatographic Conditions :** Methanol and buffer (0.02 M sodium phosphate buffer of pH 3.5 adjusted by using 0.01 M Phosphoric acid) were filtered before use. The flow rate of the mobile phase was maintained at 1 ml/minute in the ratio of 15:85 (Methanol: Buffer). The detection was carried out by UV detector a 218 nm. The data acquired was analyzed with the software class VP series version 5.03 (Shimadzu).

**Procedure :** About 100 mg of Montelukast Sodium was accurately weighed and dissolved in mobile phase so as to give a 1 mg/ml solution. Subsequent dilution of this solution was made to obtain 100 μg/ml. The standard solution prepared above was injected five times into the column at a flow rate of 1 ml/minute. The peak area for each of the drug concentrations was calculated. Montelukast Sodium solution containing 20 μg/ml and 40 μg/ml were subjected to the proposed HPLC analysis for finding out the intra-and interday variations. The recovery studies were carried out by adding a known amount of Montelukast Sodium to the pre analyzed samples, and subjecting them to proposed HPLC method.

**Estimation of Montelukast Sodium in pharmaceutical dosage forms:** An accurately weighed portion of the powder equivalent to 100 mg of Montelukast Sodium (bulk sample) was transferred to a 100 ml volumetric flask containing about 50 ml of mobile phase. The contents of the flask were sonicated to dissolve Montelukast Sodium, made up to volume with mobile phase and the resulting mixture was filtered through 0.45 μ filter. One ml of this solution was added to a 100 ml volumetric flask and made upto the volume with mobile phase. This solution 20 μl was injected five times into the column. The mean value of the peak area was calculated and the drug content in each tablet was quantified using the regression equation. The same procedure was followed for the estimation of Montelukast Sodium in six different brands of tablet dosage forms.

**Results and Discussion**

A typical chromatogram for the proposed method is shown in figure 2. The retention time for Montelukast Sodium was 3.017 minutes. Each of the samples was injected five times and the same retention time was observed in all cases. The peak areas for different concentrations are shown in table-1. The peak areas for Montelukast Sodium were reproducible as indicated by a low coefficient of variation 2.19. A good linear relationship (r = 0.9998) was observed between the concentrations of Montelukast Sodium (13, 14) and the respective peak areas. When Montelukast Sodium solution containing 20 μg/ml and 40 μg/ml were analyzed by the proposed HPLC (4, 6) method for finding out intra and interday variations, a low coefficient of variation was observed (Table-2). This shows that the present HPLC (4, 6) method is highly precise. The amounts of Montelukast Sodium from the pre analyzed samples containing known amounts of the drug are shown in Table-3. About 99.97% of Montelukast Sodium could be recovered from the pre analyzed samples indicating a high accuracy of the proposed HPLC (4, 6) method.

The absence of additional peaks indicates no interference of the excipients used in the

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The tablets were found to contain 99.98% to 100.1% of the labeled amount. The low % CV indicates the reproducibility of the assay of Montelukast Sodium in the tablet dosage form. The proposed HPLC method was found to be simple, precise, highly accurate, specific and less time consuming. Hence it is a preferred method over the reported methods for the estimation of Montelukast sodium in pharmaceutical dosage forms.

Table 1. Standard graph for the estimation of Montelukast Sodium.

<table>
<thead>
<tr>
<th>Concentration of Montelukast Sodium in (µg)</th>
<th>Peak area</th>
</tr>
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<tbody>
<tr>
<td>20</td>
<td>120.216</td>
</tr>
<tr>
<td>40</td>
<td>127.423</td>
</tr>
<tr>
<td>60</td>
<td>124.621</td>
</tr>
<tr>
<td>80</td>
<td>195.939</td>
</tr>
<tr>
<td>100</td>
<td>145.764</td>
</tr>
</tbody>
</table>

Table 2. Precision of the proposal HPLC

<table>
<thead>
<tr>
<th>Montelukast Sodium concentration (µg/ml)</th>
<th>Concentration of Montelukast Sodium (µg/ml) found on</th>
<th>Intra-day Mean (n=5)</th>
<th>% CV</th>
<th>Inter-day Mean (n=5)</th>
<th>% CV</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Mean</td>
<td></td>
<td>Mean</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>(µg/ml)</td>
<td></td>
<td>(µg/ml)</td>
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</tr>
<tr>
<td>20</td>
<td></td>
<td>20.21</td>
<td>1.89</td>
<td>20.14</td>
<td>2.50</td>
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<tr>
<td>40</td>
<td></td>
<td>40.12</td>
<td>1.25</td>
<td>40.08</td>
<td>1.88</td>
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</table>

Table 3. Recovery of Montelukast Sodium

<table>
<thead>
<tr>
<th>Amount of drug added (mg)</th>
<th>Mean (+ s.d) amount (mg) Found (n=5)</th>
<th>Mean (+ s.d) % of recovery (n=5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>20</td>
<td>20.03 ± 0.05</td>
<td>100.15 ± 0.30</td>
</tr>
<tr>
<td>40</td>
<td>39.9 ± 0.09</td>
<td>99.95 ± 0.40</td>
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</table>

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References


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