RP-HPLC METHOD FOR SIMULTANEOUS DETERMINATION OF IBUPROFEN AND FAMOTIDINE IN PHARMACEUTICAL DOSAGE FORM

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Abstract: In this study, reversed phase high performance liquid chromatographic method have been developed and validated for the simultaneous determination of ibuprofen and famotidine in combined pharmaceutical formulation. Separation was achieved with a C8 (250 mm x 4.6 mm, 5 μm) column, ambient temperature with isocratic mode with mobile phase containing acetonitrile and 0.5 M potassium dihydrogen phosphate buffer pH 2.2 adjusted with ortho-phosphoric acid (25:75). UV detection was performed at 280 nm. The flow rate was 1.2 ml/min. The retention times of ibuprofen and famotidine were found to be 3.19 min and 8.37 min, respectively. The responses were linear (R^2 > 0.9999) in the range of 20 – 160 μg/ml for ibuprofen and 0.68 – 5.4 μg/ml for famotidine. The % recovery for ibuprofen and famotidine was 99.75 and 99.24, respectively. No chromatographic interference from the tablet excipients was found. The results of the studies showed that the proposed RP-HPLC method is simple, rapid, precise and accurate, which can be applied for the routine analysis of ibuprofen and famotidine in tablet dosage forms.

Key words: liquid chromatography, validation, ibuprofen, famotidine, tablet dosage form, quality control

Introduction

The 2-arylpropionic acid derivative, ibuprofen, (RS)-2-(4-isobutyl phenyl) propionic acid is a nonsteroidal anti inflammatory drug (NSAID) which is used in reducing inflammation and pain associated with many diseases like rheumatoid arthritis, osteoarthritis and related conditions. Ibuprofen is characterized by a better tolerability compared with other NSAIDs. Famotidine is chemically 3-[(2-(diamino-methyleneamino) thiazol- 4-yl] methylthio)-N-sulfamoylpropanimidamide. It is commonly applied in the treatment of peptic ulcer disease and gastro esophageal reflux disease. Famotidine is histamine H2-receptor antagonist which blocks the action of histamine on stomach cells and reduces acid production [1, 2].

A fixed dose combined dosage form of ibuprofen and famotidine is indicated for the relief of signs and symptoms of rheumatoid arthritis and osteoarthritis and to decrease the risk of developing upper gastrointestinal ulcers. Ibuprofen is helpful in relieving the pain and inflammation associated with arthritis and famotidine reduces the risk of gastric ulcers which is a side effect in chronic usage of ibuprofen [3]. The combination of these two drugs is not official in any pharmacopoeia.

Extensive literature survey revealed determination of famotidine in dosage form by HPLC [4-10] and UV-spectrophotometry [11]. Analysis of ibuprofen in both pharmaceutical dosage forms and blood plasma has been reported by UV-spectrophotometry [12], capillary zone electrophoresis [13] and HPLC [14, 15]. Simultaneous determination of ibuprofen and famotidine in combination includes liquid chromatographic techniques [16-18], UV- spectrophotometry [19-21] and thin layer chromatography [22].

The aim of the present study is to develop an analytical method for simultaneously determination of ibuprofen and famotidine in a tablet formulation containing 400 mg ibuprofen and 13.3 mg famotidine using isocratic reversed phased liquid chromatographic procedure.

Materials and methods

Reagents and chemicals

Working standards of ibuprofen RS (Purity 100.1) and famotidine RS (purity 99.92) were provided by (Sigma-Aldrich). The formulated tablets (label claim: ibuprofen 400 mg and famotidine 13.3 mg) were used for analysis. LC-grade acetonitrile and ortho-phosphoric acid were procured from Merck (Germany). All other chemical reagents were of analytical grade.
Instrumentation and chromatographic conditions

Chromatographic separation was performed on a modular HPLC system LC-10A Shimadzu (Japan) comprising a LC-10A pump, solvent degasser DGU-3A, Rheodyne injector with 20 μl loop, column oven CTO-10A, SPD-M10A UV detector with fixed wavelength and communication bus module CBM-10A. Separation was achieved isocratically with a LiChrosorb C\text{8}, 250 mm x 4.6 mm, 5 μm column eluted with a mixture of acetonitrile and 0.5 M potassium dihydrogen phosphate buffer pH 2.5 adjusted with ortho-phosphoric acid (25:75 v/v) as the mobile phase at flow rate of 1.2 ml/min. The mobile phase was filtered through a 0.45 μm membrane filter and degassed. Detection was carried out by absorbance at 280 nm. The analysis was carried out at ambient column temperature and injection volume was 20 μl.

Preparation of reference solutions

For ibuprofen: 16 mg of ibuprofen was accurately weighed and transferred to a 50 ml volumetric flask and volume was made up to the mark with methanol (Stock solution A - 320 μg/ml).

For famotidine: 27 mg of famotidine was accurately weighed and transferred to a 100 ml volumetric flask and volume was made up to 100 ml with methanol (Stock solution B - 270 μg/ml). From Stock solution B, 5.0 ml was taken into a 50 ml volumetric flask and volume was made up to 50 ml with methanol (Stock solution C - 27 μg/ml).

For mixed standard: The reference solution was prepared by diluting 5.0 ml of stock solution A and 2.0 ml of stock solution C with methanol into a 20.0 ml volumetric flask (80 μg/ml ibuprofen and 2.7 μg/ml famotidine).

Sample preparation

Tablet’s working solution was prepared as follows: an accurately weighed quantity of powdered tablet sample containing an equivalent of 400 mg ibuprofen and 13.3 mg famotidine were transferred into 100 ml volumetric flask, then 70 ml methanol was added. The mixture was sonicated for ten minutes and the volume was made up using methanol, then the sample was filtered. 2.0 ml of the filtrate was diluted with methanol into a 100.0 ml volumetric flask to give a test solution containing 80 μg/ml ibuprofen and 2.7 μg/ml famotidine.

Results and discussion

Method validation

The proposed method was validated with respect to specificity, linearity, precision, accuracy, limit of quantitation (LOQ) and limit of detection (LOD).

Specificity

The specificity of the method was determined by checking the interference of the components against placebo. No interference was observed for any of the excipients of both drugs. The Fig. 1 showed typical chromatogram obtained from analysis of standard solution using the proposed method. The retention time observed – 3.19 min for ibuprofen and 8.37 min for famotidine permits a rapid assay, which is important for routine analysis.

Calibration and linearity

To establish the linearity of analytical method, a series of dilution in the range from 20-160 μg/ml for ibuprofen and 0.68-5.4 μg/ml for famotidine were prepared. All the solutions were filtered through 0.22 μm membrane filter prior to use and injected in chromatograph. A calibration curves were plotted between the mean peak areas vs. respective concentrations. The corresponding linear regression equation was \( y=10784x-1320.2 \) with square of correlation coefficient \( R^2 \) of 0.9999 for ibuprofen and \( y=18540x-1264.4 \) with square of correlation coefficient \( R^2 \) of 0.9999 for famotidine, respectively.

Limit of quantitation and limit of detection

The limit of quantitation and limit of detection were calculated from the standard deviations and slopes of the responses using a signal-to-noise ratio. The LOQs for ibuprofen and famotidine were found to be 2 μg/ml and 0.8 μg/ml, while the LODs were 0.2 μg/ml and 0.1 μg/ml, respectively.
Accuracy
Recovery studies were performed to validate the accuracy of developed method. To the preanalysed sample solution, a definite concentration of standard drug was added and then its recovery was analysed. The percent recovery for ibuprofen was found to be 99.75% and for famotidine it was 99.24%. Results presented in Table 1 indicated good accuracy and showed no interference from tablet excipients.

Precision
The precision of the method was evaluated by performing six independent determinations of the test sample preparation and calculating RSD (%). The RSD values measured during assessment of precision was <2.0% for both analytes, confirming the method is precise (Table 2).

Conclusion
The statistical data have been proven that developed HPLC procedure for simultaneous estimation of ibuprofen and famotidine was found to be accurate, precise, and sensitive. Therefore the proposed method can be applied for routine quality control analysis.

Table 1. Statistical data for accuracy

<table>
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<th>Statistical data</th>
<th>ibuprofen</th>
<th>famotidine</th>
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<tr>
<td>% Recovery</td>
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<td>99.24</td>
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<tr>
<td>SD*</td>
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<td>% RSD</td>
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*Average value of three determinations, RSD is relative standard deviation

Table 2. Precision of the method

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*Mean of three determinations

References


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