Original Article

RP-UPLC method development and validation for the simultaneous estimation of ibuprofen and famotidine in pharmaceutical dosage form

Abstract

Aim and Backrgound: A stability-indicating LC method was developed for the simultaneous determination of Ibuprofen and Famotidine in pharmaceutical dosage forms. **Materials and Methods:** The chromatographic separation was achieved on Acquity UPLC BEH C-18,50 mm x 2.1 mm and 1.7 µm column with gradient elution. The mobile phase A contains a mixture of 50 mM sodium acetate buffer (pH 5.5): methanol (85:15, v/v), and the mobile phase B contains a mixture of 50 mM sodium acetate buffer (pH 5.5): methanol (25:75, v/v). The flow rate was 0.3 mL min^{-1}, and the detection wavelength was 260 nm. **Results:** The limit of detection for Ibuprofen and Famotidine was 1.6 and 1.2 µg mL^{-1}, respectively. The limit of quantification (LOQ) for Ibuprofen and Famotidine was 5.1 and 4.3 µg mL^{-1}, respectively. **Conclusion:** This method was validated for accuracy, precision, and linearity. The method was also found to be stability indicating.

Key words: Famotidine, ibuprofen, ssimultaneous, sstability-indicating, UPLC

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INTRODUCTION

Famotidine (FM), 3-(((2-((aminoiminomethyl)amino)-4-thiazolyl)methyl)thio)-N′-(aminosulfonyl) propanimidamide is a potent, competitive, and reversible inhibitor of histamine action at the H_2 receptor. It is used for the treatment of duodenal and gastric ulcers. The empirical formula of Famotidine is $C_8H_{15}N_7O_2S_3$ and its molecular weight is 337.43. Famotidine is available in 20 mg and 40 mg for oral administration.[1]

Ibuprofen (IB) ((2*RS*)-2-[4-(2-Methylpropyl)phenyl]propanoic acid) is a non-steroidal anti-inflammatory drug, which is available in 400 mg, 600 mg, and 800 mg tablets for oral administration. It is indicated for relief of the signs and symptoms of rheumatoid arthritis and osteoarthritis for relief of mild to moderate pain and also indicated for the treatment of primary dysmenorrhea. The empirical formula for Ibuprofen is $C_{13}H_{18}O_2$ and its molecular weight is 206.29.[2]

To the best of our knowledge, few liquid chromatography procedures were described for the individual determination of Ibuprofen [Figure 1a] and Famotidine [Figure 1b].[2-17] These procedures were developed to estimate either Ibuprofen or Famotidine individually and from formulation or plasma, whereas no single method has been reported for their simultaneous estimation from the formulation. Hence, it is necessary to develop a stability indicating, rapid, accurate, and validated LC method for the simultaneous determination of Ibuprofen and Famotidine from combined dosage form for generic drug development.

Ultra performance liquid chromatography (UPLC) is a recent technique in liquid chromatography, which enables significant reductions in separation time and solvent consumption. Literature indicates that UPLC system allows about

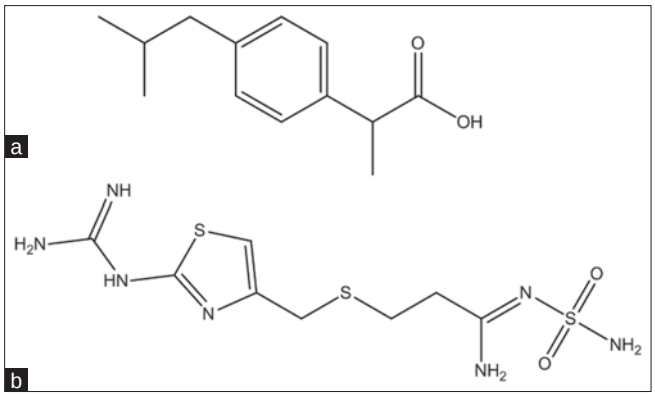

Figure 1: Chemical structure and chemical name of (a) Ibuprofen (b) Famotidine.

9-fold decreases in analysis time as compared to the conventional HPLC system using 5 μm particle size analytical columns, and about 3-fold decrease in analysis time in comparison with 3 μm particle size analytical columns without compromise on overall separation.

EXPERIMENTAL

Apparatus

Acquity UPLCTM system (Waters, Milford, USA) used consisting of a binary solvent manager, a sample manager and a UV detector. The output signal was monitored and processed using empower software, water bath equipped with MV controller (Julabo, Seelbach, Germany) was used for hydrolysis studies. Photo stability studies were carried out in a photo stability chamber (Sanyo, Leicestershire, UK). Thermal stability studies were performed in a dry air oven (MACK Pharmatech, Hyderabad, India).

Reagents and chemicals

Ibuprofen and Famotidine (Duexis) tablets (800 mg of Ibuprofen and 26 mg of Famotidine) were purchased from the pharmacy. Sodium acetate trihydrate, triethylamine, glacial acetic acid, methanol for HPLC were purchased from Merck, Darmstadt, Germany, and water used was obtained by using Millipore MilliQ Plus water purification system

Chromatographic conditions

The chromatographic column used Acquity UPLC BEH C-18,50 mm x 2.1 mm and 1.7 μm particle size. The separation was achieved on a gradient method. The buffer used for mobile phase and diluent was 0.05 M sodium acetate buffer and 2 ml of triethyl amine in 1000 ml of water and adjusted the pH to 5.5 with glacial acetic acid. Mobile phase A was a mixture of pH 5.5 buffer and methanol in the ratio of 85: 15(v/v), respectively, and the mobile phase B contains a mixture of pH 5.5 buffer and methanol in the ratio of 75:25 (v/v), respectively. The flow rate of mobile phase was set as 0.3 Ml min^{-1}. The UPLC gradient program was set as: Time (min)/% solution B: 0.01/10,1.6/100, 2.8/100, 3.0/10, and 3.5/10. The column temperature was maintained at 25°C, and the detector was monitored at a wavelength 260 nm. The injection volume was 1.5 μL.

Preparation of stock solutions

A standard solution containing 1600 μg/ml of IBU and 50 μg/ml of FAM were prepared by dissolving IB and FM in diluent (50:50 (v/v) pH 5.5 sodium acetate buffer and methanol).

Preparation of sample solution

Twenty tablets, each containing 800 mg of IB and 26 mg of FM, were weighed individually to determine the average weight and powdered separately in a mortar. A quantity of powder equivalent to 52 mg of FM and 1600 mg of IB were weighed and transferred into a 500 ml volumetric flask, added 300 ml of diluent and sonicated for 45 minutes with intermediate shaking and then made up to volume with diluent.

RESULTS AND DISCUSSION

Method development and optimization of stability indicating assay method

The method was optimized to separate major degradation products formed under varies stress conditions. I (pKa = 4.4) is acetic compound, whereas FM (pKa = 7.1) is basic compound. The main target of the chromatographic method is to get the separation for closely eluting degradation products. The degradation samples were run using different stationary phases like C18, C8, Cyano, and mobile phases containing buffers like phosphate, sulfate, and acetate with different pH (2-7) and using organic modifiers like acetonitrile and methanol in the mobile phase. But, the separation was satisfactory in the adopted chromatographic conditions only [Table 1 and Figure 2] the optimized conditions are, the mobile phase A was a mixture of pH 5.5 buffer and methanol in the ratio of 85:15(v/v), respectively, and the mobile phase B contains a mixture of pH 5.5 buffer and methanol in the ratio of 75:25 (v/v), respectively.

Specificity – forced degradation studies

Forced degradation studies were performed on IB