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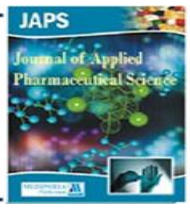

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Simultaneous Estimation of Ibuprofen and Famotidine in Pure and Combination Dosage Form by RP-HPLC

Narendra Nyola and Govinda Samy Jeyabalan

Narendra Nyola
Department of Pharmaceutical Sciences, Shridhar University, Pilani, Rajasthan, India.

Govinda Samy Jeyabalan
Department of Analytical Chemistry Research Laboratory, Alwar Pharmacy College, Alwar, Rajasthan, India.

For Correspondence
Narendra Nyola
Email: narennyola2@gmail.com

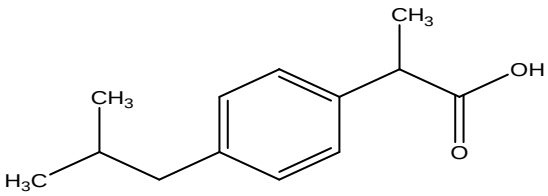
ABSTRACT

A new simple, accurate, precise and reproducible RP-HPLC method has been developed for the simultaneous estimation of ibuprofen and famotidine in tablet dosage forms using C_{18} column (Phenomenex, 250 x 4.6 mm, 5 µm) in isocratic mode. The mobile phase consisted of Methanol: Water: Phosphate buffer in the ratio of 70:20:10 (v/v/v). The flow rate was 1.0 ml/min and detection wavelength was carried out at 284 nm. The retention times of ibuprofen and famotidine were 3.6 min and 7.8 min, respectively. The method was linear over the concentration range for ibuprofen 2-10 µg/ml and for and famotidine 2-10 µg/ml. The recoveries of ibuprofen and famotidine were found to be in the range of 99.037-100.766% and 99.703-100.433% respectively. The validation of method was carried out utilizing ICH-guidelines. The described HPLC method was successfully employed for the analysis of pharmaceutical formulations containing combined dosage form.

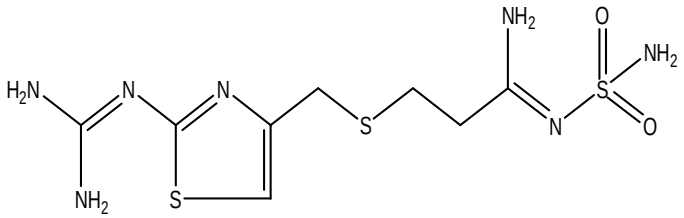
Keywords: Simultaneous estimation, RP-HPLC, ibuprofen, famotidine.

INTRODUCTION

Ibuprofen (IB) is (*RS*)-2-(4-isobutylphenyl) propionic acid. Its Mol. Formula $C_{13}H_{18}O_2$ Mol. Wt. 206.3 is a non-steroidal anti-inflammatory medication used especially for the relief of the symptoms of arthritis, primary dysmenorrhoea and fever, and as an analgesic, especially where there is an inflammatory component. Its side effects are gastrointestinal haemorrhage and ulceration (Clarke's Analysis of Drugs and Poisons, 2004; Rang *et al.*, 2003 ; Merck Index, 1994; Indian Pharmacopoeia, 2007).



Ibuprofen



Famotidine

Famotidine (FTD) is chemically 3-[({2-[(diaminomethylidene) amino]-1, 3-thiazol-4-yl} methyl) sulfanyl] - N' sulfamoyl propanimidamide. (Clarke's Analysis of Drugs and Poisons, 2004; Rang *et al.*, 2003) FTD is official in British Pharmacopoeia (BP, 2009) and United state Pharmacopoeia. It has an empirical formula $C_8H_{15}N_7O_2S_3$ and a molecular weight of 337. (United USP, 2004) The FTD is an H_2 blocker that works by reducing the amount of acid produced by the stomach because IB has a tendency to cause ulcers; FTD is added in combination to reduce the risk for ulcers (Merck Index, 1994). The combination dosage form of IB and FTD is available in the market and it is indicated in the treatment of Osteoarthritis and Rheumatoid arthritis. Because IB has a tendency to cause ulcers, FTD is added in combination to reduce the risk for ulcers.

A literature survey regarding quantitative analysis of these drugs revealed that attempts have been made to develop analytical methods for the estimation of IB alone and in combination with other drugs by liquid chromatographic (LC) (Reddy *et al.*, 2009), UPLC–MS/MS (Szeitz *et al.*, 2010), HPTLC (Chitlange *et al.*, 2008; Sam *et al.*, 2010; Rele *et al.*, 2010) , super critical fluid chromatography (Bari *et al.*, 1997) and spectrophotometric methods (Gondalia *et al.*, 2010), kinetic spectrophotometry (Snezana *et al.*, 2008) potentiometric indications(European Pharmacopoeia 2002) . For FTD Literature survey revealed that liquid chromatographic (LC) (Najma *et al.*, 2011), HPTLC (Novakovic,1999) and spectrophotometric methods (Kanakapura *et al.*, 2011) have been reported for the estimation of FTD.

However there is no method reported for the simultaneous estimation of these drugs in combined dosage forms. Fixed dose combination containing IB (800 mg) and (FTD 26.6 mg) is available in the tablet form in the market. The aim of this work was to develop an HPLC method for the simultaneous estimation of IB and FTD in pharmaceutical dosage forms. The present method was validated as per ICH guidelines (ICH, 2005).

EXPERIMENTAL

Apparatus

The liquid chromatographic system consists of shimadzu 20 AT UFLC with UV-VIS detector, binary pump and rheodyne injector valve with 20 µl fixed loop. The analytes were monitored at 284 nm. Chromatographic analysis was performed on Phenomenex C_{18} column having 250 mm× 4.6 mm i.d. and 5 µm particle size. Chromatogram was automatically obtained by spinchrome system software.

Reagents and Materials

All chemicals and reagents were used of AR grade. Authentic of IB and FTD were obtained as gift samples from A to Z Pharmaceutical Chennai. Tablet formulation containing labelled amount of 800 mg of IB and 26.6 mg of FTD was used for the study.

Selection of detection wavelength

Solution of each drug in acetonitrile was scanned over the range of 200-400 nm. It was observed that both the drugs showed considerable absorbance at 284 nm was selected as the wavelength for detection.(fig.1)

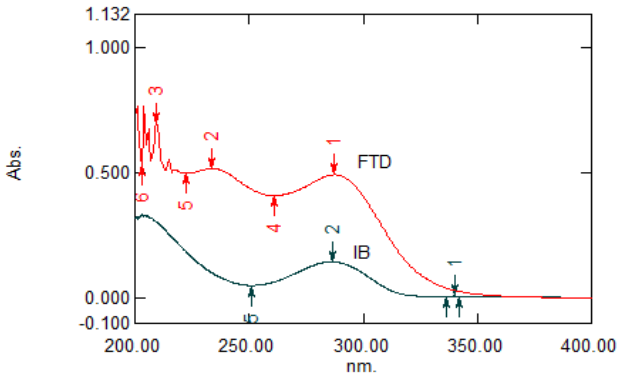


Fig. 1: Uv Spectra Of Ib And Ftd.

Chromatographic Conditions

The Phenomnex C_{18} column (250 x 4.6mm, 5µm) equilibrated with mobile phase Methanol: Water: Phosphate buffer in the ratio of 70:20:10 (v/v/v) was used. The flow rate was maintained at 1 ml/min. Detection wavelength with UV detector at 284 nm, and the injection volume was 20 µl and run time was kept 10 min.

Preparation of standard stock solutions

IB and FTD were weighed (50 mg each) and transferred to two separate 50ml volumetric flasks and dissolved in 20 ml of methanol and make up the volume up to the mark with distilled water and the final concentration of solution containing 1000 µg/ml of IB and FTD, respectively.

Preparation of working solutions

Aliquot from the stock solutions of IB and FTD were appropriately diluted with distilled water to obtain working standard of IB and FTD.

METHOD DEVELOPMENT

Lots of mobile phase and there different proportions were tried and finally was selected as Methanol: Water: Phosphate buffer in the ratio of 70:20:10 (v/v/v) appropriate mobile phase which gave good resolution and acceptable system suitability parameters.The chromatogram of working standard solution is shown in fig 2.

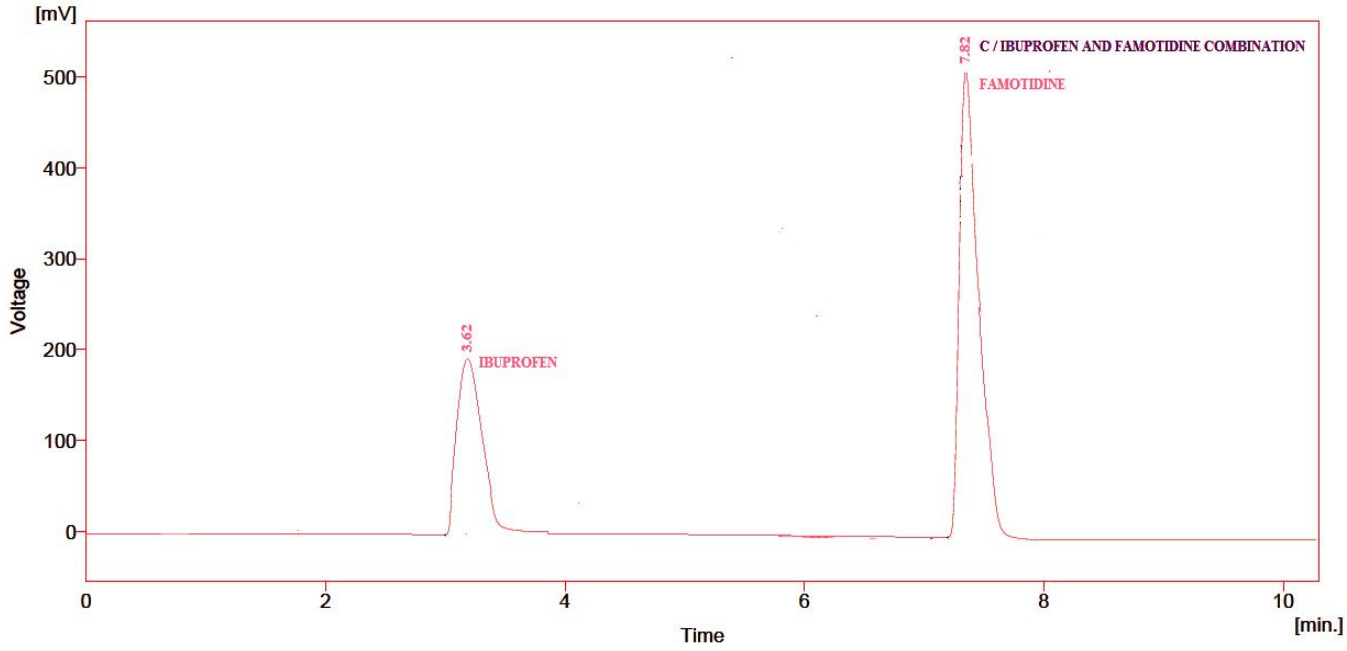


Fig . 2: Chromatograms Of Ib And Ftd.

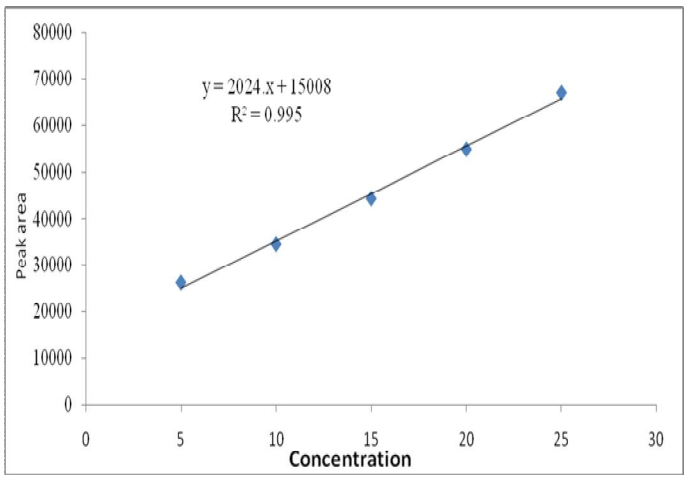


Fig. 3: Calibration Curve of Ib.

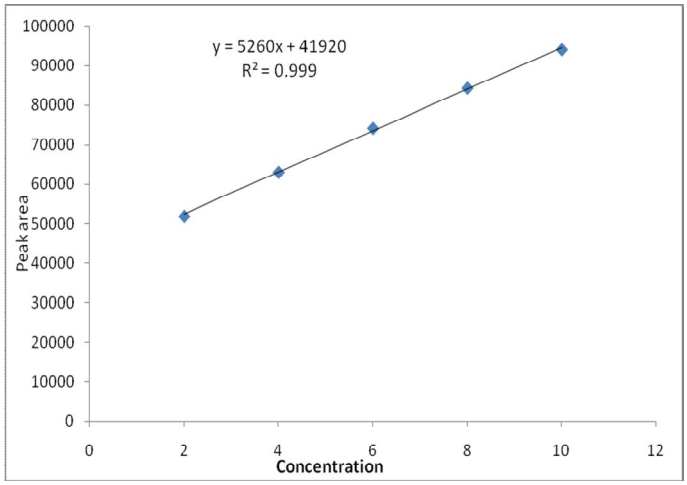


Fig. 4: Calibration Curve of Ftd.

Calibration curve

Accurately measured volumes of working standard solution of IB and FTD were transferred into a series of 10ml volumetric flasks and diluted appropriately with mobile phase. 20µl of each solution was injected at same chromatographic conditions. Calibration curves were obtained by plotting the peak area versus concentration of drug. Regression equations were calculated. The method was found linear over a concentration range 5-25µg/mL of IB and 2-10µg/mL of FTD. (Fig. 3, 4)

Precision

The repeatability studies were carried out by estimating response of IB (10 µg/mL) and FTD (6 µg/mL) five times and results are reported in terms of % CV. The intra-day and inter-day precision studies were carried out by estimating the corresponding responses five times on interday and intraday for three different concentrations of IB (5, 10, 15 µg/ml) and FTD (2, 4, 6 µg/ml), and It is expressed as the percentage coefficient of Variation (% CV) which is calculated as per the following expression % CV = (standard deviation / mean) x 100.

Accuracy

Accuracy of method was observed by recovery result from 3 placebos preparations accurately spiked with different concentration of the active ingredient.

Recovery assessment was obtained by using standard addition technique which was by adding known quantities of pure standards at three different levels in 80%, 100% and 120% to the pre analysed sample formulation. From the amount of drug found, amount of drug recovered and percentage recovery were calculated which sense to conformation that the proposed method was accurate.

Analysis of marketed formulation

Ten tablets were weighed accurately and finely powdered. Tablet powder equivalent to 800 mg IB and 26.6 mg of FTD was taken in 100 ml volumetric flask. Methanol (20 ml) was added to the above flask and the flask was sonicated for 30 minutes. The solution was filtered using whatman filter paper No.1 and volume was made up to the mark with distilled water. From this solution prepare working solutions they have concentration 10µg/ml of IB and 6µg/ml of FTD.

Detection Limit

The Detection Limit of an individual analytical procedure is the lowest amount of analyte in a sample which can be detected but not necessarily quantitated as an exact value. The detection limit (LOD) may be expressed as:

$$LOD = \frac{3.3\sigma}{S}$$

Where

σ = Relative standard deviation of the response.

S = the slope of the calibration curve (of the analyte).

Quantitation Limit

The Quantitation limit of an analytical procedure is the lowest amount of analyte in a sample, which can be quantitatively determined with suitable precision and accuracy.

Quantitation Limit (LOQ) may be expressed as:

$$LOQ = \frac{10\sigma}{S}$$

Where

σ = Relative standard deviation of the response.

S = the slope of the calibration curve (of the analyte).

Specificity

The method was determined as specific by comparing test results obtained from analyses of sample solution containing placebo ingredients with that of test results those obtained from analyses of standard solution.

RESULTS AND DISCUSSION

The present work done on this combination comprises a simple, precise and accurate method by reverse phase high performance liquid chromatography. The present combination of IB and FTD was marketed as one formulation. An attempt has been made to estimate IB and FTD by RP-HPLC. Even though number methods have been reported earlier for IB and FTD individually and with other combinations, an effort has been made to identify a common mobile phase to come up with the isocratic elution of both drugs in combination. Calibration curve depicting the linearity and range for IB and FTD were determined from mixed standards and were found to be of the order 5-25 µg /ml of IB and 2-10 µg /ml of FTD. The formulation was diluted in the linearity range and peak areas were determined, the concentrations of both like IB and FTD were then determined by comparing the peak areas of sample with that of standard peak areas of IB and FTD in mixture can be identified by their retention times being 3.6 minutes for IB and 7.8 minutes for FTD. The results obtained from HPLC method were reproducible and encouraging. The values percentage deviation was within limit (>2%) and recovery close to 100% indicating reproducibility and accuracy of method.

Table. 1: Analytical parameters for the determination of IB and FTD .

S.No.	PARAMETERS	IBUPROFEN	FAMOTIDINE
1	Limit of linearity (µg/ml)	5-25	2-10
2	Regression equation	y = 2024.1x + 15008	y = 5260x + 41920
3	Slope	337.33	5260
4	Intercept	1500.8	41920
5	Correlation coefficient (r)	0.9951	0.9991
6	Retention time (min)	3.6	7.8
7	Detection limit (µg/ml)	2.592	0.418
8	Quantitation limit (µg/ml)	8.641	1.393
9	Accuracy (%)	99.84	100.076
10	Precision (% CV)		
	Intra-day precision (n=5)	0.152	0.084
	Inter-day precision (n=5)	0.078	0.079
11	Theoretical plates	4887	3203

CONCLUSION

The developed methods were validated as per ICH guidelines and were found to be within the prescribed limit. It concludes that the developed methods are simple, accurate, sensitive and precise and suitable for both authentic and tablet dosage form.

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