INTRODUCTION

Ibuprofen (IBPA) 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.\(^{1,3}\)

Famotidine (FOD) is chemically 3-[(2-[(diaminomethylidene) amino]-1, 3-thiazol-4-yl] methyl sulfonyl] – N sulfamoyl propanimidamide\(^{1-2}\). FOD is official in British Pharmacopoeia and United state Pharmacopoeia. It has an empirical formula C_{13}H_{13}N_{2}O_{5}S and a molecular weight of 337.\(^{4,5}\) The FOD is an H\(_2\) blocker that works by reducing the amount of acid produced by the stomach because IBPA has a tendency to cause ulcers, FOD is added in combination to reduce the risk for ulcers.\(^{2}\) The combination dosage form of IBPA and FOD is available in the market and is indicated in the treatment of Osteoarthritis and Rheumatoid arthritis. Because IBPA has a tendency to cause ulcers, FOD 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 IBPA alone and in combination with other drugs by liquid chromatographic (LC)\(^{6-9}\), UPLC–MS/MS\(^{7}\), HPTLC\(^{8-10}\), super critical fluid chromatography\(^{11}\)and spectrophotometric methods \(^{12}\), kinetic spectrophotometry\(^{13}\) potentiometric indications\(^{14,15}\). For FOD Literature survey revealed that liquid chromatographic (LC)\(^{14}\), HPTLC\(^{16}\) and spectrophotometric methods\(^{17}\) have been reported for the estimation of FOD. However there is no method reported for the simultaneous estimation of these drugs in combined dosage forms. Fixed dose combination containing IBPA (800 mg) and (FOD 26.6 mg) is available in the tablet form in the market. The aim of this work was to develop a uv-vis method for the simultaneous estimation of IBPA and FOD in pharmaceutical dosage forms. The present method was validated following ICH guidelines.\(^{18}\)

EXPERIMENTAL APPARATUS

A shimadzu model 1800 double beam UV/ Visible spectrophotometer with spectral width of 1 nm, wavelength accuracy of ± 0.1 nm and a pair of 10 mm matched quartz cell was used to measure absorbance of all the solutions. Spectra were automatically obtained by UV-Probe system software.

REAGENTS AND MATERIALS

All chemicals and reagents were used of AR grade. Authentic of IBPA and FOD were obtained as gift samples from Glenmark Pharmaceutical Mumbai. Tablet formulation containing labelled amount of 800 mg of IBPA and 26.6 mg of FOD 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 224 nm for IBPA and 286 nm for FOD was selected as the wavelength for detection.

PREPARATION OF STANDARD STOCK SOLUTIONS

IBPA and FOD were weighed (100 mg each) and transferred to two separate 100ml 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 \(\mu\)g/mL of IBPA and FOD, respectively.

PREPARATION OF WORKING SOLUTIONS

Aliquot from the stock solutions of IBPA and FOD were appropriately diluted with distilled water to obtain working standard 100 \(\mu\)g/ml of IBPA and FOD.

METHOD VALIDATION

The method was validated for accuracy, precision, linearity, detection limit, quantitation limit and robustness.
LINEARITY
Appropriate aliquots of IBPA and FOD working standard solutions were taken in different 10 mL volumetric flasks and diluted up to the mark with mobile phase to obtain final concentrations of 4, 8, 12, 16, 20 μg/mL of IBPA and 2, 4, 6, 8, 10 μg/mL of FOD, respectively. Calibration curves were constructed by plotting absorbance versus concentrations and regression equations were calculated for both the drugs.

PRECISION
The repeatability studies were carried out by estimating response of IBPA (12 μg/mL) and FOD (6 μg/mL) six times and results are reported in terms of relative standard deviation. The intra-day and inter-day precision studies (intermediate precision) were carried out by estimating the corresponding responses 3 times on the same day and on 3 different days for three different concentrations of IBPA (8, 16, 20 μg/mL) and FOD (4, 6, 10 μg/mL), and the results are reported in terms of relative standard deviation.

ACCURACY
The accuracy of the method was determined by calculating recoveries of IBPA and FOD by method of standard additions at three different levels 80, 100 and 120 %. Mean percentage recovery was determined. Recovery values were calculated and shown in Table 2.

ANALYSIS OF MARKETED FORMULATION
Twenty tablets were weighed accurately and finely powdered. Tablet powder equivalent to 800 mg IBPA and 26.6 mg of FOD 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.41 and volume was made up to the mark with distilled water. From this solution prepare working solutions they have concentration 16μg/mL of IBPA and 6μg/ml of FOD.

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:

\[
\text{LOD} = \frac{3.3\sigma}{S}
\]

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:

\[
\text{LOQ} = \frac{10\sigma}{S}
\]

Where
σ = Relative standard deviation of the response.
S = the slope of the calibration curve (of the analyte).

SPECIFICITY
The specificity of the method was ascertained by peak purity profiling studies. Purity of the drug peak was ascertained by analyzing the spectra.

CONCLUSION
Proposed study describes method for the estimation of IBPA and FOD combination in mixture. The method was validated and found to be simple, sensitive, accurate and precise as per ICH guidelines. The method was successfully used for determination of drugs in their pharmaceutical formulation.

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REFERENCES
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| TABLE 2 ASSAY OF COMBINED DOSAGE FORMBRAND USED |
|--------------------------|------------------|------------------|-----------------|------------------|
| DRUG                     | LABEL CLAIM (mg/TABLET) | AMOUNT ESTIMATED (mg/TABLET)* | PERCENTAGE LABEL CLAIM (%) | % DEVIATION |
| IBUPROFEN                | 800               | 794              | 99.25            | -0.75          |
| FAMOTIDINE               | 26.6              | 26.48            | 99.54            | -0.46          |

*Mean of five reading

| TABLE 3 RECOVERY STUDIES |
|--------------------------|--------------------------|
| AMOUNT OF DRUG SAMPLE USED IBUPROFEN | THEORETICAL AMOUNT ADDED (%) | OBTAINED (µg) IBUPROFEN | %RECOVERY | AMOUNT OF DRUG SAMPLE USED FAMOTIDINE | OBTAINED (µg) FAMOTIDINE | %RECOVERY |
| 12µg                     | 80                       | 9.5               | 98.95      | 6µg                        | 4.85                        | 101.03     |
| 12µg                     | 100                      | 12.20             | 101.6      | 6µg                        | 6.10                        | 101.6      |
| 12µg                     | 120                      | 14.20             | 98.6       | 6µg                        | 7.15                        | 99.3       |
| MEAN % RECOVERY          |                          | 99.76             |            | MEAN % RECOVERY            | 100.64                      |
| SD                       |                          | 1.64              |            | SD                         | 1.19                        |
| %RSD                     |                          | 1.64              |            | %RSD                       | 1.18                        |

*Mean of three determinations in each level
FIGURE 3 CALIBRATION CURVE OF IBUPROFEN

FIGURE 4 CALIBRATION CURVE OF FAMOTIDINE

FIGURE 5 UV-VIS SPECTRA OF IBUPROFEN

FIGURE 6 UV-VIS SPECTRA OF FAMOTIDINE

FIGURE 7 UV-VIS SPECTRA OF IBUPROFEN FAMOTIDINE

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