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ORIGINAL RESEARCH ARTICLE

Development and Validation of Spectrophotometric Method for Determination of Flurbiprofen in Bulk and Formulation

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ABSTRACT

Flurbiprofen, a propionic acid derivative, is a non-steroidal anti- inflammatory (NSAID) with antipyretic In present study, a simple, rapid, accurate, and economical UV-spectrophotometric method has been developed for the estimation of flurbiprofen from bulk and pharmaceutical formulation. The developed method was statistically validated in accordance with ICH requirement on the basis of various parameters like linearity, accuracy, precision, sensitivity, repeatability and ruggedness. The drug follows linearity in the concentration range 2-12 µg/ml in methanol with a correlation coefficient value of 0.999 at λ_{max} of 247 nm . The accuracy of the method was checked by recovery experiment performed at three different levels, i.e., 80%, 100%, and 120%. The % recovery was found to be in the range of 100.98- 101.54%. The precision of the method was studied as an intraday; interday variations, and repeatability. The % RSD value < 2 indicates that the method is precise, reproducible and accurate. Ruggedness of the proposed method was also studied with the help of two analysts. The proposed method was then successfully applied to pharmaceutical formulation. Amount of drug estimated was found to be 99.29-100.52%, which was in good agreement with the label claim. Excipients used in tablet formulation did not interfere in the estimation of flurbiprofen by developed method. The proposed method can be successfully employed in the routine analysis of drug in pharmaceutical dosage forms.

Key Words: Analysis, Dosage forms, Formulation, Flurbiprofen, Quantitative determination, UV, Validation.

INTRODUCTION

Flurbiprofen, a propionic acid derivative, is a non-steroidal anti- inflammatory (NSAID) with antipyretic and flurbiprofen may be used for the symptomatic treatment of rheumatoid arthritis and alkylosing spondylitis, used topically prior to ocular, surgery to prevent or reduce intraoperative miosis [1]. Flurbiprofen is also used as an active ingredient in some kinds of throat lozenges (Strepsils Intensive) Chemically it is (RS)-2-(2-fluorobiphenyl-4-yl) propanoic acid derivative (**Fig 1**) with empirical formula of $C_{15}H_{13}FO_2$. and molecular weight of 244. 26. Literature survey reveled that methods for estimation on the basis of liquid chromatography, [2] LC-MS/MS, stability indicating assays and HPTLC [3] have been reported previously. Recently very few spectrophotometric methods [4] were also reported for estimation of flurbiprofen but a validated analytical method with industrial acceptance remains need of hour . Hence an attempt was made to develop and validate a simple and reproducible spectroscopy based analytical method for its determination in bulk and pharmaceuticals formulation as per ICH guidelines [5.6].

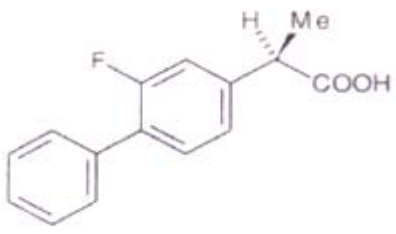

Fig 1: Chemical structure of flurbiprofen

MATERIALS AND METHODS

Flurbiprofen was obtained from Sun Pharma LTD, Ahemadnagar, as a gift sample. The chemical

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chemical structure and purity of drug obtained were confirmed by TLC, IR, melting point, DSC and XRD studies. Marketed tablets (Anasid 100 mg) were purchased from the local market. All chemicals and reagents used were of analytical grade and purchased from Merck, India. A Perkin Elmer double beam UV/Visible Spectrophotometer with 1 cm matched pair of rectangular quartz cells were employed to measure absorbance.

Preparation of standard stock solution

Accurately weighted 20 mg of drug was dissolved in 10 ml of methanol. The volume was made up to 100 ml with methanol. This solution served as stock solution, and various dilutions were prepared from 2 to 12 µg/ml concentration. The absorbance of the resulting solution is determined at 247 nm using spectrophotometrically against methanol as a blank. The standard curve between concentration (µg/ml) and absorbance was plotted. These standard curves were linearly regressed and statistical parameters were applied.

Selection of wavelength for analysis of flurbiprofen

Appropriate volume of standard stock solution of flurbiprofen (0.5 ml) was transferred into a 10 ml volumetric flask, diluted to a mark with methanol to give concentration of 5 µg/ml. The resulting solution was scanned in the UV range (200-400 nm). A typical spectrum obtained from standard solution is shown in (**Fig 2**).

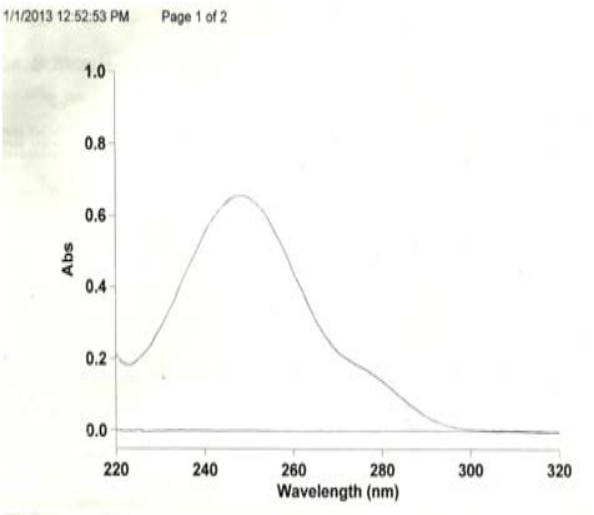

Fig 2: UV spectrum of flurbiprofen at 247 nm

Validation of the method

The method was validated in terms of linearity, accuracy, precision, sensitivity, repeatability and ruggedness.

For linearity studies, daily working standard solution of flurbiprofen were prepared by suitable dilution of the stock solution with methanol. Six sets of analyte solution were prepared containing flurbiprofen at a concentration of 2,4,6,8,10 and 12 µg/ml. The standard solutions were scanned at 247 nm for corresponding absorbance. The calibration curve for flurbiprofen was constructed by plotting the mean absorbance of 6 replicates (Y-axis) against the concentration (X-axis). In order to determine accuracy, a known amount of standard stock solution was added to the preanalysed sample solutions at different levels, i.e. 4, 6 and 8 µg. The solutions were then reanalyzed by the proposed method for drug content. Precision of the method was studied as intraday and interday variations. Intraday precision was determined by analyzing flurbiprofen standard solutions (4, 6 and 8µg/ml) for three times in the same day. Interday precision was determined by analyzing sample standard of the flurbiprofen solutions daily for 3 days over the period of week. The sensitivity of analytical measurements of flurbiprofen by the use of the proposed method was estimated in terms of the limit of quantification (LOQ) and limit of detection (LOD). The LOQ and LOD were calculated using equation LOD = 3.3 × *N*/*B* and LOQ = 10 × *N*/*B*, where '*N*' is standard deviation of the peak areas of the drugs (n = 6), taken as a measure of noise, and '*B*' is the slope of the corresponding calibration curve. Repeatability was determined by analyzing a particular concentration of Flurbiprofen for six times i.e.6 µg/ml. Ruggedness of the developed method was determined for 6 µg/ml concentration of flurbiprofen by analysis of aliquots from a homogenous slot by two analysts using same operational and environmental conditions.

Determination of Flurbiprofen in bulk

Accurately weighed quantity of flurbiprofen (10 mg) was transferred into a 100 ml volumetric flask containing 20 ml methanol and the volume was made up to the mark using the same. Appropriate volume of this solution was transferred to a 10 ml volumetric flask and the volume was adjusted to the mark using methanol. The resulting solution was scanned on a spectrophotometer in the UV range 200-400 nm. The concentrations of the drug were calculated from linear regression equations.

Application of the proposed method for pharmaceutical formulation

For analysis of commercial formulation, thirty tablets were taken and accurately weighted. Then

tablets were crushed to a fine powder. The powdered sample, equivalent to 10 mg of flurbiprofen, was transferred to a 100 ml volumetric flask and about 20 ml of methanol was added and sonicated to dissolve. The volume was made up to the mark with methanol (100 µg/ml), then an aliquot of this solution (0.6 ml) was transferred to a 10 ml volumetric flask and made up to a sufficient volume with methanol to get desired concentration of 6 µg/ml. This solution was filtered through Whatman filter paper. It was scanned on a spectrophotometer in the UV range 200-400 nm. The spectrum was recorded at 247 nm and the concentrations of the drug were calculated using from the corresponding absorbance the linear regression equation.

RESULTS AND DISCUSSION

Method validation

The proposed method was validated as per ICH guidelines. The solutions of the drugs were prepared as per the earlier adopted procedure given in the experiment.

Linearity studies

The linear regression data for the calibration curve, as shown in (**Fig 3**), demonstrated good linear relationship over the concentration range 2-12µg/ml for Flurbiprofen. The results are shown as (**Table 1**). Linear regression equation was found to be y = 0.0324x + 0.008 (r^2 = 0.999).

Table 1: Linearity study of flurbiprofen

Concentration (µg/ml)	Average Absorbance (Mean ±S.D.)	%RSD
2	0.160±0.014	0.602
4	0.321±0.060	0.602
6	0.485±0.130	0.602
8	0.632±0.029	0.602
10	0.792±0.011	0.602
12	0.950±0.036	0.602

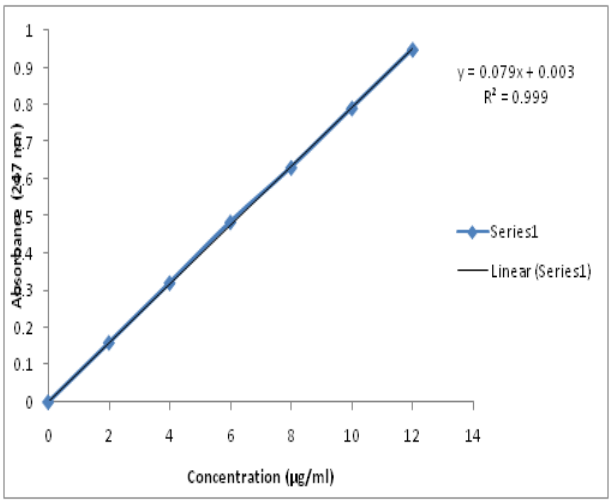

Fig 3: Calibration curve of flurbiprofen at 247 nm

Accuracy

Accuracy of proposed method was checked by performing recovery studies using standard addition method. The solutions were reanalyzed after spiking by the proposed method; results of recovery studies are given in (**Table 2**), which showed that the % amount found was between 100.98% and 101.54 % with % RSD > 2.

Table 2: Recovery studies

Concentration of pre-analyzed sample solution (µg/ml)	Amount of drug added (µg/ml)	Amount recovered[a] (µg/ml)	% Recovery
6	2	08.17	101.08
	4	10.20	100.98
	6	13.42	101.54

[a] Average of three estimates.

Precision

The precision of the developed method was expressed in terms of % relative standard deviation (% RSD). These results show reproducibility of the assay. The % RSD values found to be less than 2 that indicate this method precise for the determination of both the drugs in formulation (**Table 3**).

Table 3: Precision studies

Concentration of drug (µg/ml)	Intraday precision[a]		Interday precision[a]	
	Conc. found	%RSD	Conc. found	%RSD
04	3.96	0.045	3.93	0.302
06	6.6	0.401	5.87	0.338
08	7.93	0.301	7.96	0.300

[a] Average of three estimates.

Sensitivity

The linearity equation was found to be 'y = 0.0324x + 0.0082'. The LOQ and LOD for flurbiprofen by developed method were found to be 0.42 µg and 1.30 µg respectively.

Repeatability

Repeatability was determined by analyzing 6 µg/ml concentration of flurbiprofen solution for six times and the average % amount found was 100.66±0.048% with % RSD < 2 (**Table 4**).

Table 4: Repeatability studies

Component	Amount taken (µg/ml)	Amount found (%)[a]	% RSD
Flurbiprofen	6	100.66±0.048	0.324

[a] Average of six estimates.

Ruggedness

It was studied by measuring peak area for solutions of same concentration determinations were done by different analysis for six times each. The results are given in (**Table 5**)**.** The result showed that the % RSD was less than 2%, which was in acceptable range as per ICH guidelines.

Table 5: Ruggedness studies

Component	Amount taken (µg/ml)	Amount found (%)[a]	
Flurbiprofen	6	Analyst I (%±SD)	Analyst II (%±SD)
		99.04±1.3	98.90±0.95

[a] Average of six estimates.

Determination of flurbiprofen in bulk

The concentrations of the drug were calculated from linear regression equations. The % amount found was between 99.64% and 100.10%.The results are given in (**Table 6**).

Table 6: Analysis of flurbiprofen in bulk

Concentration (µg/ml)	Amount found (µg)[a]	Amount found (%)
6	05.94737	99.64
	05.97368	99.82
	05.96362	99.75
	05.81053	99.73
	05.97302	99.82
	05.01631	100.10
Mean±SD	05.94±0.070	99.81±0.150
%RSD	0.468	0.450

Determination of flurbiprofen in pharmaceutical formulation

Content of flurbiprofen in tablet formulation were calculated from the linear regression equation obtained in linearity studies. The results are given in (**Table 7**). The % amount found was between 99.29% and 100.52%.

Table 7: Analysis of flurbiprofen in formulation

Concentration (µg/ml)	Amount found (µg)[a]	Amount found (%)
6	5.89472	99.29
	5.97328	99.82
	5.90211	99.34
	5.97365	99.82
	5.94637	99.64
	5.07895	100.52
Mean±SD	5.96±0.066	99.73±0.445
%RSD	0.441	0.446

[a] Average of six replications

CONCLUSION

The results obtained in the present study indicated that the developed method for estimation of Flurbiprofen by spectrophotometric means is simple, accurate, precise and reproducible as per ICH guidelines. This method also showed high specificity in the presence of formulation excipients and has permitted quantification of drug over linearity in the range of 2-12 µg/ml. Thus the proposed method can be used as cost effective method for routine analysis of flurbiprofen in bulk and pharmaceutical formulations.

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