RESEARCH ARTICLE

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Stability Indicating Analytic Method Development for Estimation of Ibuprofen Formulation Using RP HPLC Method

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Abstract: The main aim and focus of present study was to develop RP-HPLC method and validation in stability indicating manner as per ICH guidelines for the quantification of ibuprofen in pharmaceutical formulations. Ibuprofen is commonly used as non steroidal anti inflammatory drug (NSAID) to achieve higher pharmacological activity. The optimized chromatographic conditions includes a C-18 RP-HPLC column as stationary phase and the mobile phase pumped with the flow rate of 1.0 ml/min and the eluent was monitored at 220 nm were established. The mobile phase contains a combination of buffer and acetonitrile in the ratio of 40:60% (v/v). The developed method is a simple, rapid, precise, specific and accurate for the determination of ibuprofen in the range of 20% to 200% of working concentrations.

INTRODUCTION

Ibuprofen, a propionic acid derivative, is a prototypical nonsteroidal anti-inflammatory agent (NSAIDs) with analgesic and antipyretic properties. Ibuprofen is a widely used as NSAID (Non Steroidal Anti Inflammatory Drug) in a racemic mixture. [1] Ibuprofen (IB) ((2*RS*)-2-[4-(2-Methylpropyl) phenyl] propanoic acid). The empirical formula for ibuprofen is $C_{13}H_{18}O_2$ and its molecular weight is 206.29 which is available in 400 mg, 600 mg, and 800 mg tablets for oral administration. [2-3]

Ibuprofen is sued for symptomatic treatment of rheumatoid arthritis, juvenile rheumatoid arthritis and osteoarthritis. Also used to treat mild to moderate pain and for the management of dysmenorrheal, reduces fever, treatment of ankylosing spondylitis, gout and psoriatic arthritis. [4-6]

Few liquid chromatography procedures were described for the individual determination of ibuprofen these procedures were developed to estimate ibuprofen individually and from formulation or plasma, whereas no single method has been reported for their simultaneous estimation from the formulation.

The main aim of the present work was to develop stability indicating RP-HPLC method for the quantitative estimation of ibuprofen in pharmaceutical formulations such as tablet, extrude and gel dosage forms etc. S(+)-Ibuprofen form is not official in any pharmacopoeias but literature survey reveals that there are limited techniques for the estimation of ibuprofen in tablet form using HPTLC, UV Spectrophotometric methods and few HPLC methods in plasma and urine samples. As per literature no article reported on unique method for quantitative estimation of ibuprofen from different dosage. [7-9]

MATERIALS AND METHODS

Ibuprofen working standard grade was supplied by Cadilla Healthcare Ltd., Ahmedabad, India. Water (HPLC Grade), Methanol (HPLC Grade), Acetonitrile (HPLC Grade) and all other chemicals/solvents used were of analytical grade and collected from the Local market.

Selection of Detection Wavelength

The sensitivity of HPLC method that uses UV detection depends upon proper selection of detection wavelength. An ideal wavelength is the one that gives good response for the drugs that are to be detected. In the present study drug solution of 100 µg/ml was, therefore, prepared in solvent methanol. This drug solution was than scanned in the UV region of 200-400 nm and the spectrum was recorded.

Preparation of Stock Solution

The stock solution was prepared by weighing accurately 10 mg Ibuprofen and transferred into a clean and dry 100 ml volumetric flask. About 70 ml of diluent was added and sonicated. The volume was made upto the mark with the same diluent. From the above prepared Stock solution pipette out 0.49 ml and 1.5 ml of solution and transferred into a clean and dry 10 ml volumetric flask, the diluent was added upto the mark to get final concentration.

Preparation of Sample Solution

The sample solution was prepared by weighing equivalently 10 mg of ibuprofen and transferred into a 100 ml clean and dry volumetric flask and about 70 ml of diluent was added and sonicated to dissolve it completely and the volume made up to the mark with the same solvent. From above prepared stock solution pipette out 1.5 ml of solution and transferred into a clean and dry 10 ml volumetric flask, the diluent was added upto the mark 10 ml to get final concentration. The standard and sample solutions were injected five times and the peak areas were recorded. The mean and percentage relative standard deviation were calculated from the peak areas.

Method Validation

1. Linearity and Range

Linearity was determined at five levels over the range of 20% to 150% with respect to the test concentration. A standard stock solution was prepared by taking 500 mg of working standard in a 50 ml of diluent (10,000 ppm) and further diluted to attain concentration of about 20%, 50%,

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Table 1: Linearity Study of Drug at 264 nm in HPLC

Levels	ml. Added	Diluted to (ml)	Conc. (ppm)	Area
LOQ	1.0	1.0	997.0000	---
LEVEL-1	2.0	50.0	399.1988	610307.000
LEVEL-2	5.0	50.0	997.9970	1487028.000
LEVEL-3	10.0	50.0	1995.9940	2955078.000
LEVEL-4	6.0	25.0	2395.1928	3524527.000
LEVEL-5	7.5	25.0	2993.9910	4402072.000

Table 2: Determination of Method Precision (Repeatability)

Sets	Test Weight (mg)	Test Reading	Mg/Tab	% Assay	Mean % Assay	%RSD
1	498.40	2870614	491.42	98.60	98.97	0.21
2	504.30	291552	498.75	98.90		
3	497.30	2882253	493.32	99.20		
4	491.90	2846344	486.98	99.00		
5	496.10	287059	491.13	99.00		
6	499.10	2890506	494.60	99.10		

Table 3: Data Derived from Chromatogram for the +5°C Temperature (50°C)

Name	Retention Time	Area	% Area	Theoretical Plates	Asymmetry
Ibuprofen	3.808	2962642	100	6855.45	1.24

Table 4: Data Derived from Chromatogram for the -5°C Temperature (40°C)

Name	Retention Time	Area	% Area	Theoretical plates	Asymmetry
Ibuprofen	3.957	2960754	100	7158.61	1.26

Table 5: Data Derived from Chromatogram for the +10% Flow Rate (1.1 ml/min)

Name	Retention Time	Area	% Area	Theoretical Plates	Asymmetry
Ibuprofen	3.509	2683792	100	6998.81	1.38

Table 6: Data Derived from Chromatogram for the -10% Flow Rate (0.9 ml/min)

Name	Retention Time	Area	% Area	Theoretical plates	Asymmetry
Ibuprofen	4.331	3324795	100	7148.45	1.35

Table 7: Data Derived from Chromatogram for the +2% Absolute Organic Phase Ratio [Organic Phase: ACN (42: 58)]

Name	Retention Time	Area	% Area	Theoretical Plates	Asymmetry
Ibuprofen	3.616	2962016	100	6648.40	1.30

Table 8: Data Derived from Chromatogram for the -2% Absolute Organic Phase Ratio [Organic Phase: ACN (38: 62)]

Name	Retention Time	Area	% Area	Theoretical Plates	Asymmetry
Ibuprofen	4.181	2963641	100	7432.81	1.29

100 %, 120% and 150% of sample concentration. The area at each level was calculated and a graph was plotted by taking area on Y-axis and concentration (%) on X-axis. The correlation co-efficient (r), y-intercept, slope of regression line and residual sum of squares were calculated and recorded in Table 1.

2. Precision

Method precision was established by assaying six sample preparations under same conditions. Individual assay values mean assay value, % RSD was calculated and recorded in Table 2.

The Chromatograms of the same are given in Figure 2.

3. Accuracy (Recovery)

The accuracy of the analytical method for assay of drug was established at three levels in triplicate, viz. 50%, 100% and 150% of the test concentration. Standard was prepared as per method.

4. Robustness

The robustness of the method was established by making deliberate minor variations in the following method parameters:

1. Column temperature: ±5.0°C
2. Flow rate: ±10.0%
3. Organic phase ratio: ±2.0% Absolute.

Table 9: Data Derived from Robustness Experiment

Parameters		% RSD	Theoritical Plates	Assymetry
Normal Conditions		0.050	6935.54	1.10
Temperature	40°C	0.070	7158.61	1.26
(45°C)	50°C	0.019	6855.45	1.24
Flow Rate	0.9 ml/min	0.083	7148.45	1.35
(1 ml/min)	1.1 ml/min	0.133	6998.91	1.38
Mobile Phase (2 % absolute)	38:62	0.059	7432.81	1.29
As buffer: ACN	42:58	0.069	6648.40	1.30

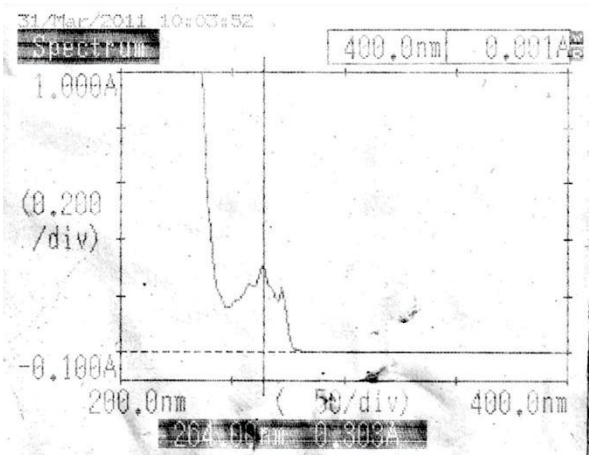

Figure 1: Selection of detection wavelength

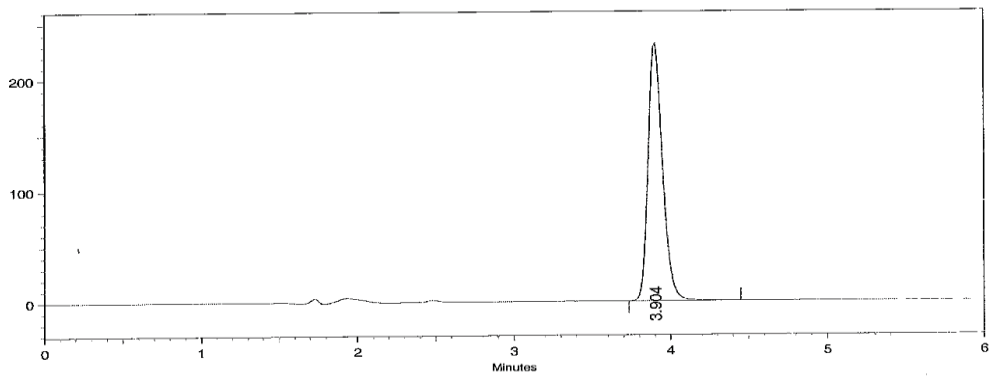

Figure 2: Chromatogram of method precision at 100 % Level

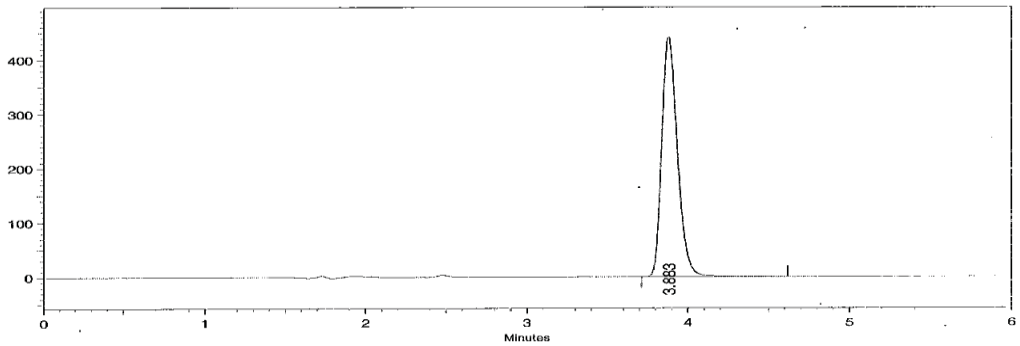

Figure 3: Chromatogram of Standard under normal conditions

Blank, standard preparation and sample preparation were prepared and injected. The effect of changes observed on system suitability parameters, theoretical plates and asymmetry were recorded in Table 3 to Table 8. The Chromatograms of the same are given in Figure 3 to Figure 8.

RESULTS AND DISCUSSION

The present work was undertaken with the aim to develop and validate a rapid and consistent RP-HPLC method development in which the peaks will be appear with short period of time as per ICH Guidelines. The proposed method was simple, fast, accurate and precise method for the

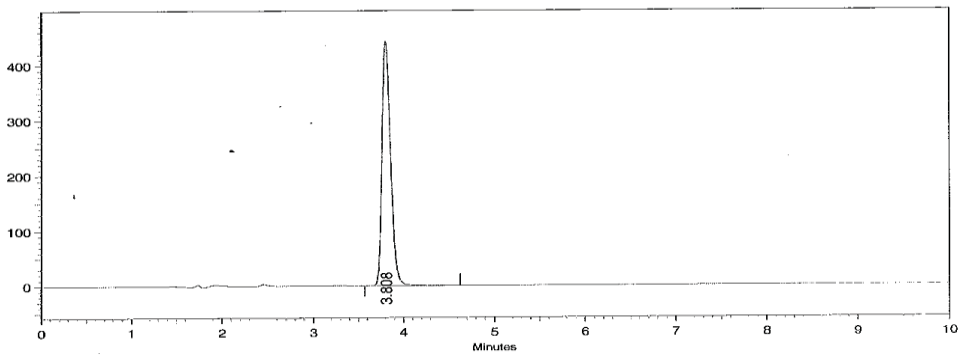

Figure 4: Chromatogram of standard at +5°C column temp. (50°C)

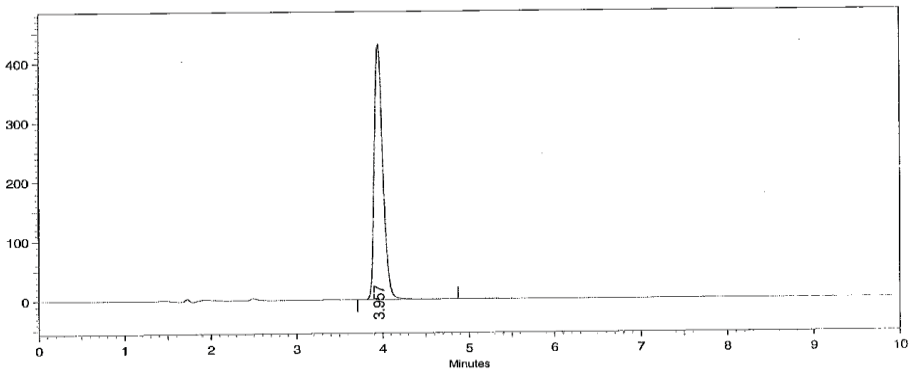

Figure 5: Chromatogram of standard at -5°C column temp. (40°C)

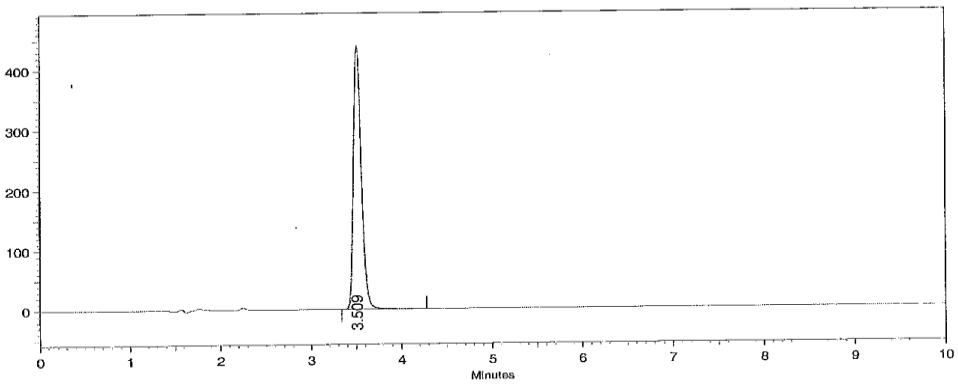

Figure 6: Chromatogram of standard at +10 % flow rate (1.1ml/min)

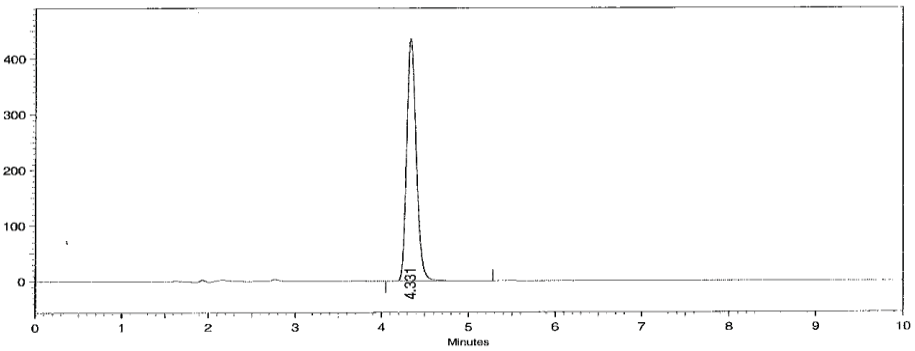

Figure 7: Chromatogram of standard at -10 % flow rate (0.9 ml/min)

Quantification of drug in the Pharmaceutical dosage form, bulk drug as well as for routine analysis in Quality control. Overall the proposed method was found to be suitable and accurate for the Quantitative determination of the drug in tablet dosage form.

The method was simple, precise, accurate and sensitive and applicable for the simultaneous determination of Ibuprofen in bulk drug and in combined dosage forms. The High performance liquid chromatography (RP-HPLC) methods was developed and validated for simultaneous

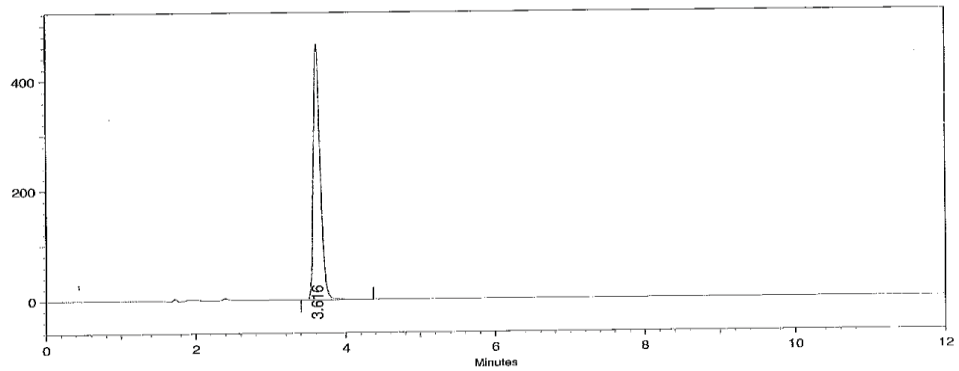

Figure 8: Chromatogram of standard at +2 % absolute organic phase ratio [Organic Phase: ACN (42: 58)]

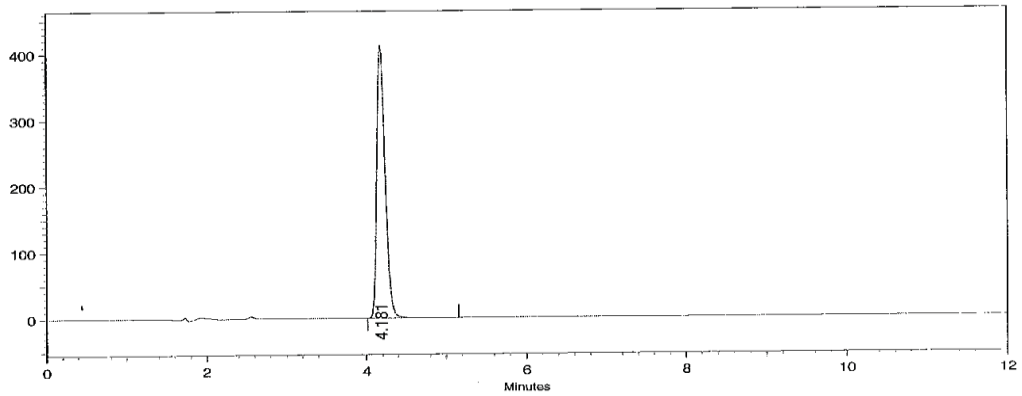

Figure 9: Chromatogram of standard at -2 % absolute organic phase ratio [Organic Phase: ACN (38: 62)]

estimation of ibuprofen in bulk drug and in combined dosage forms. The RP-HPLC separation was achieved on a Symmetry C18 (2.1 x 100 mm, 1.7 µm, Make: BEH) or equivalent in an isocratic Mode. The mobile phase was composed of Phosphate Buffer (30%) whose pH was adjusted to 4.0 by using TEA and Acetonitrile [HPLC Grade] (70%). The flow rate was monitored at 1.2 ml per min. The wavelength was selected for the detection was 264 nm. The run time was 8min. The retention time found for the drugs Ibuprofen.

The Precision data for the drugs Ibuprofen were represented. The %RSD for sample should be NMT 2. The %RSD for the standard solution was found for the drugs Ibuprofen which is within the limits hence the method was precise.

The standard solution with Accuracy - 50%, Accuracy - 100% and Accuracy - 150% were injected into chromatographic system and calculated the amount found and amount added for Ibuprofen and further calculated the individual recovery and mean recovery values.

CONCLUSION

Based on the results obtained from the analysis of forced degraded samples using described method, it was concluded that there were no other co-eluting peaks of interference from excipients and degradation products due to variable stress components with the main peaks and the method was specific for the estimation of Ibuprofen in presence of various degradants. So previously described method can be used as stability indicating method for assay of Ibuprofen.

REFERENCES AND NOTES

1. Sweetman and Sean. Martindale, The complete drug reference. Pharmaceutical Press, London, 37th Edition, April 2011.
2. http://www.rxlist.com/ibuprofen-drug.htm.
3. http://www.rxlist.com/pepcid-drug.htm.
4. Zawada E T Jr. Renal consequences of nonsteroidal antiinflammatory drugs. Postgrad Med, 71(5):223-30, 1982.
5. Townsend K P, Pratico D. Novel therapeutic opportunities for Alzheimer's disease: focus on nonsteroidal anti-inflammatory drugs. FASEB J, 19(12):1592-601, 2005.
6. Chen H, Jacobs E, Schwarzschild M A, McCullough M L, Calle E E, Thun M J, Ascherio A. Nonsteroidal antiinflammatory drug use and the risk for Parkinson's disease. Ann Neurol, 58(6):963-7, 2005.
7. Muralidharan S, Meyyanathan S N. Validated HPTLC method ofanalysis of Dexibuprofen in its formulation, Jr of Planar Chromatography – Modern TLC, 22(3):207-210, 2009.
8. P G Dhartarkar, R V Kalamkar, S D Saoji, G Ingle, S C Atram, Madhuri D Game. Development and validation of uv spectrophotometric method for estimation of dexibuprofen in bulk and dosage form. Der Pharma Chemica, 3(4):361-366, 2011.
9. A D Hulst, P Augustijns, S Arens. Determination of artesunate by capillary electrophoresis with low UV detection and possible applications to analogues. Journal of Chromatographic Science, 34(6):276-281, 1996.

Cite this article as: Jahangir Ali, Mahesh Kumar Gupta, Neetesh Kumar Jain *et al*. Stability Indicating Analytic Method Development for Estimation of Ibuprofen Formulation Using RP HPLC Method. Inventi Rapid: Pharm Analysis & Quality Assurance, 2015(1):1-5, 2014.