UV SPECTROPHOTOMETRIC METHOD OF IBUPROFEN IN PHARMACEUTICAL DOSAGE FORM BY USING MULTIVARIATE CALIBRATION CURVE TECHNIQUE

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Abstract

An accurate and precise UV spectrophotometric method with a multivariate calibration technique for the determination of Ibuprofen in pharmaceutical formulations has been described: The multivariate technique is a process of constructing a mathematical model that relates a property such as content or identity to the absorbance of a set of known reference samples at more than one wavelength. This technique is based on the use of linear regression equations by using the relationship between concentration and absorbance at five different wavelengths 219,221,223, 225, and 227nm. The ibuprofen shows absorption maxima at 223 nm and obeyed Beer's law in the 4-20 µg/ml range. The results were treated statistically and were found to be highly accurate, precise, and reproducible. This statistical approach gives optimum results for eliminating fluctuations coming from instrumental or experimental conditions. It was concluded that the proposed method is simple, easy to apply, economical, and could be used as an alternative to the existing spectrophotometric and non-spectrophotometric methods for the routine analysis of Ibuprofen in pharmaceutical formulations.

Introduction

Ibuprofen (IBF) is, an effective oral antipyretic, analgesic, and non-steroidal anti-inflammatory drug (NSAID) that is widely used to treat a variety of conditions, including postoperative pain, dental pain, dysmenorrhea, osteoarthritis, and rheumatoid arthritis[1]. It is well known that the majority of NSAIDs prevent prostaglandin synthesis and the enzyme COX (cyclooxygenase). It is chemically named 2-(4-Isobutylphenyl) propanoic acid. The relative inhibitory effectiveness of traditional NSAIDs against COX isoforms, specifically COX-1 and COX-2, varies. This decreased topical irritating activity appears to be primarily caused by masking of the ibuprofen-free carboxylic group. Ibuprofen has been changed into several heterocyclic amide derivatives that have been shown to have better analgesic properties and fewer side effects. One such amide derivative is aminoprofen, which has been used topically to treat inflammation. A survey of the literature reveals that ibuprofen's spectrophotometric estimation in tablet dose form has been documented.[2-10]. Multivariate calibration with biased regression techniques is a powerful tool for analytical chemistry, of possible use in many problems of pharmaceutical analysis, both in the case of direct analysis in complex matrices and multi-component analysis in simple systems.[11-12] If the absorbance of an analyte (Z) is measured at five wavelengths set, a straight-line equation can be written as; $A\lambda = aX(Cz+k)$ where $A\lambda$ represents the absorbance of the analyte, A is the slope, and k is the intercept of the linear regression function of the analyte. CZ represents the concentration of the analyte. At five selected wavelengths, the equation system can also be summed as; A T = aX (CZ + b) X (CZ +c) X (CZ + d) X (CZ +e) X (CZ +KT), which can be simplified to AT = CZ (a+b+c+d+e) +KT where a, b, c, d, e are the slopes, AT and K T represents the sum of absorbance obtained and the sum of intercepts of regression equations at five wavelengths set respectively. The concentration of the Z analyte in a mixture can be calculated by using the Eqn. CZ = AT -KT /(a+b+c+d+e). This paper describes the application of UV spectral multivariate calibration technique having simple mathematical content for the quantitative determination of ibuprofen in pharmaceutical formulation.

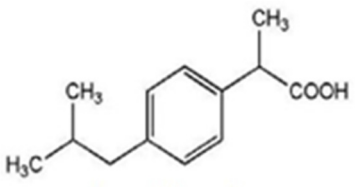

Figure 1. Structure of Ibuprofen

Materials and Methods

Chemicals

The Ibuprofen gift sample from Alpha Drugs Limited (Hyderabad). The commercial pharmaceutical formulations were obtained from local Pharmacies.

Instrumentation

The multivariate technique was performed in a UV-visible spectrophotometer (Labman Instruments Ltd.) 1.0cm quartz cells using

Preparation of Standard Solutions

The standard solution (1000 µ g/ml) was prepared by accurately weighing 100 mg of ibuprofen in a 100 mL volumetric flask containing 50 mL of Methanol and water and sonicated for about 5 min, and then the volume was made up to the mark with methanol and water. From this 10 mL was pipetted out into a 100 mL volumetric flask and the volume was made up to the mark with methanol and water to get a final concentration of 100 µg/ml.

Preparation of sample solution

For analysis of marketing formulations, twenty tablets were weighed accurately and powdered. The powder equivalent to 100mg of the drug weighed accurately and transferred to a 100mL volumetric flask containing 50mL of methanol and water. The mixture was sonicated to dissolve, and make up the volume with methanol and water. The above solutions were filtered through Whatman filter paper and the solution was transferred into a volumetric flask and was made up to the mark with methanol and water to obtain a final concentration of 20 µg/ml. All determinations were conducted with six replicates.

Method Validation

The method was validated according to the International Conference on Harmonization (ICH) Q2B guidelines17 for validation of analytical procedure to determine the linearity, limit of detection, limit of quantitation, accuracy, and precisions.

Linearity

Linearity was established by least squares linear regression analysis of the calibration curve. The constructed calibration curves were linear over the concentration range of 4-20 µg/ml for Ibuprofen. Absorbance is plotted versus their respective concentrations and linear regression analysis is performed.

Precision

Precision was determined as intra-assay and inter-assay, by ICH guidelines. The intra-day and inter-day precision were determined by analyzing the samples of ibuprofen. The low %RSD values obtained from the analysis of tablets indicated that the method was highly precise.

Accuracy

The accuracy of the proposed method was determined using recovery studies by the standard addition method. The recovery studies were carried out by adding different amounts (50, 100, and 150%) of the pure drug to the pre-analysed formulation. The solutions were prepared in triplicates and the % recovery was calculated.

%Recovery= Amount found /amount added × 100

Limit of Detection and Limit of Quantitation

The limit of quantification (LOQ) and limit of detection (LOD) were based on the residual standard deviation of the response and the slope of the constructed calibration curve (n=3), as described in the International Conference on Harmonization guidelines Q2 (R1).

LOD = 3.3 × σ/S, LOQ = 10 × σ/S

Where σ = the standard deviation of the response and

S = the slope of the calibration curve Multivariate calibration.

Molar extinction coefficient (ε)

It is a measure of how strongly a chemical species or substance absorbs light at a particular wavelength

$$A = \varepsilon Lc$$

A =is the amount of light absorbed by the sample for a particular wavelength

ε = the molar extinction coefficient

L = the distance that the light travels through the solution

c is the concentration of the absorbing species per unit volume

Rearrange the Beer-Lambert equation to solve for the molar extinction coefficient:

$$\varepsilon = A/Lc$$

Sandell ‘s sensitivity

For sensitivity measurement of UV spectrophotometry analytical method, Sandell's sensitivity was calculated using the following formulas:

$S=10^{-3}/\varepsilon_S$

$\varepsilon_S = \varepsilon x 1000/$Molecular weight of determinant

Results and discussions

The validation sets consisting of six solutions in a working range of 4-20 µg/mL were freshly prepared and scanned in the UV region. The absorbance was recorded and plotted calibration curve against concentration, which followed Beer’s law and gave a straight line. To improve this correlation and minimize instrumental fluctuations, absorbances of these solutions were measured over a range surrounding 223nm i.e., 219,221,225,227nm. The calibration curves of ibuprofen at different wavelengths.

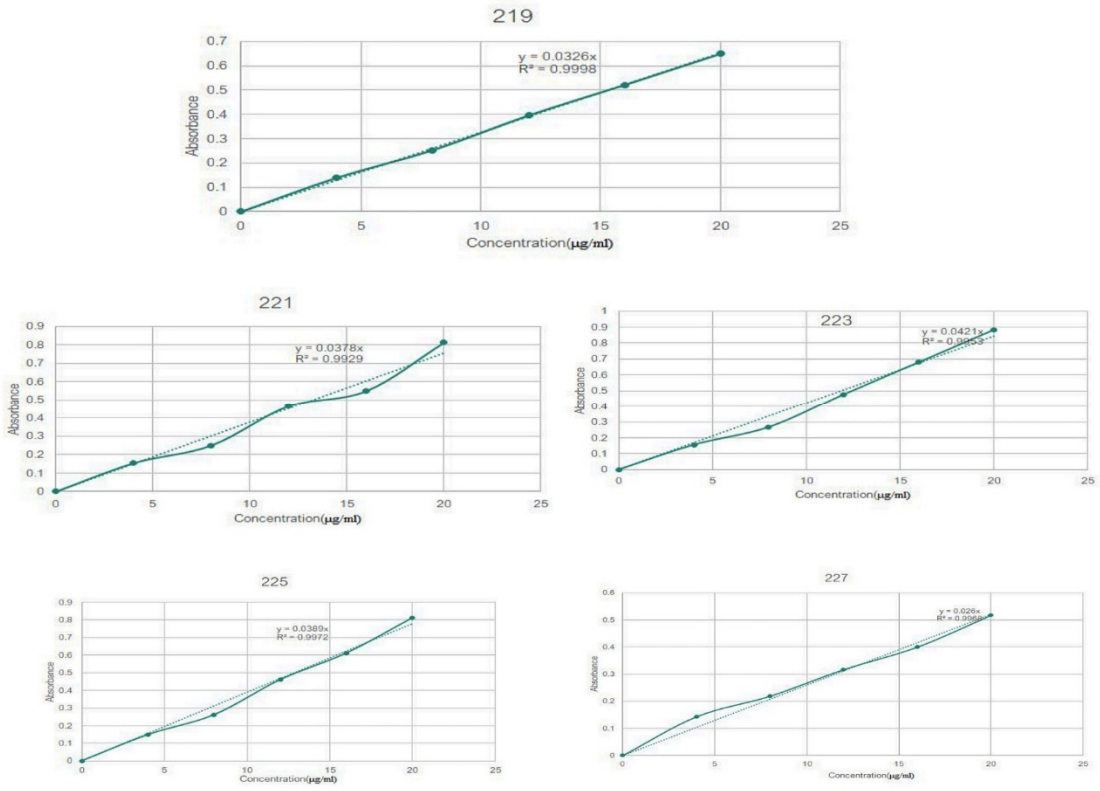

Figure 3. Calibration curve data of ibuprofen at different wavelengths

To check the degree of repeatability of the method, a suitable statistical evaluation was carried out. The concentration of a drug is measured six times on the same day at intervals of 1hr and on six different days for intra and inter-day study, respectively. The Relative Standard Deviation (% RSD) was less than 2.

Table 1. Results of Precision

Concentration (µg/ml) (n=6)	Intra-day precision		Inter-day precision	
	Abs mean ± S.D (n=6)	%RSD	abs mean± S.D (n=6)	%RSD
4	0.445 ±0.00320	1.123	0.447±0.00324	0.981

The percentage recovery values were found to be 98.27 - 102.01 with a %RSD of <2, which indicates that the proposed method was accurate.

Table 2. Results of Accuracy

Spiked level (%)	Formulation Concentration (µg/ml)	Pure Drug Concentration (µg/ml)	Amount found	% Recovery	%Mean recovery ±SD	%RSD
50 %	4	2	6.01	100.0	99.9±0.353	0.561
	4	2	6.00	100.0		
	4	2	5.98	99.60		
100 %	4	4	8.00	100 .0	99.9±0.189	0.241
	4	4	7.99	99.7		
	4	4	8.02	100.0		
150%	4	6	10.0	100.0	100.0±0.011	0.158
	4	6	10.1	100		
	4	6	10.1	100		

Table 3. Analysis of Formulation

Drug	Label Claim (mg/Tablet)	Amount Estimated (mg/Tablet)	%Label Claim (Mean+ Sd)	RSD
Ibuprofen	400.0	396.0	99.2±0.21	0.441

Ibuprofen was estimated by the proposed multivariate UV spectrophotometric method in tablets. It was completely soluble in methanol and hence methanol was selected as the solvent for ibuprofen to obtain a UV spectrum in the range of 220-400 nm. After the evaluation of the spectrum, ibuprofen presented maximum absorbance at 223nm.

Table 4. Summary of the proposed method of ibuprofen by using different parameters

Parameters	219nm	221nm	223nm	225nm	227nm
Beers law range(µg/mL)	4-20	4-20	4-20	4-20	4-20
Molar extinction co-efficient(1/mol/cm)	0.035	0.038	0.039	0.037	0.035
Sandell's sensitivity (µg/cm^2)	0.169	0.186	0.189	0.179	0.169
Limit of detection (µg/mL)	0.5	0.4	0.3	0.4	0.6
Limit of quantitation(µg/mL)	1.53	1.32	1.12	1.28	2.02
Intercept	0.0029	0.0184	0.032	0.0208	0.0193
Slope	0.0324	0.039	0.0443	0.0403	0.0247
Correlation coefficient (r^2)	0.998	0.9929	0.9901	0.9972	0.9929

Multivariate Calibration Calculations

$A\ \lambda\ 219 = a*C_x + k1$

$A\ \lambda\ 221 = b*C_x + k2$

$A\ \lambda\ 223 = c*C_x + k3$

$A\ \lambda\ 225 = d*C_x + k4$

$A\ \lambda\ 227 = e*C_x + k6$

219=0.9994*60+0.0326 =59.9966 ---------[1]

221=0.9929*60+0.0378 =59.6118----------[2]

223=0.9901*60+0.0421 = 59.4481---------[3]

225=0.9972*60+0.0389 =59.8709----------[4]

227=0.9929*60+0.026 =59.6----------[5]

$A_T=a*C_x+b*C_x+c*C_x+d*C_x+e*C_x$---------[6]

The above equation can be further condensed to $A_T=C_x(a+b+c+d+e)+K_T$----------[7]

Where A_T and K_T are the summations of the absorbance acquired cum totality intercept of the regressions equations at selected 5 wavelengths respectively. The concentration of the analyte X is computed by the following formula**.**

$C_x=A_T-K_T/(a+b+c+d+e)$
$C_x=298.5298-0.1774/4.97254 =298.3524/4.97254$
$C_x=60$

Conclusion

The proposed method is rapid, accurate, precise, and sensitive for the quantification of ibuprofen from its pharmaceutical dosage forms by the multivariate spectrophotometric method. The method relies on the use of a simple working procedure comparable to that achieved by sophisticated and expensive techniques like HPLC, and hence this method can be routinely employed in quality control for analysis of ibuprofen in tablets.

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