

Development and Validation of Spectrophotometric Methods for Simultaneous Estimation of IBUPROFEN and PARACETAMOL in Soft gelatin capsule by Simultaneous Equation Method

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Abstract: A simple, rapid, accurate, precise, specific and economical spectrophotometric method for simultaneous estimation of Ibuprofen and Paracetamol in combined soft gelatin capsule dosage form has been developed. It employs formation and solving of simultaneous equation using two wavelengths 224.0 nm and 248.0 nm. This method obeys Beer's law in the employed concentration ranges of 4-14 $\mu\text{g/mL}$ and 2-12 $\mu\text{g/mL}$ for Ibuprofen and Paracetamol, respectively. Results of analysis were validated statistically and by recovery studies.

Key words: Ibuprofen, Paracetamol, Simultaneous Equation.

Introduction

The 2-arylpropionic acid derivative, Ibuprofen [RS-2-(4-isobutyl-phenyl)propionic acid], is one of the most potent orally active antipyretic, analgesic and nonsteroidal anti-inflammatory drug (NSAID) used extensively in the treatment of acute and chronic pain, osteoarthritis, rheumatoid arthritis and related conditions. This compound is characterized by a better tolerability compared with other NSAIDs^[1]. Ibuprofen contains a chiral carbon atom on the propionic acid side-chain, therefore it exists as two enantiomers. It is usually marketed as a 50:50 mixture of the *S*- and *R*-enantiomers, even if it is known that the pharmacological activity is due almost exclusively to the *S*- enantiomer^[2].

Paracetamol is 4'-Hydroxyacetanilide. It is antipyretic and analgesic. Paracetamol alone or in combination with other drugs is reported to be estimated by spectrophotometric method, HPLC, TLC, HPTLC, LC-MS, FT-IR, Amperometric determination,

Fluorimetry and Micellar electrokinetic chromatographic method^[3].

Spectrophotometric methods are reported, the individual and in combination for estimation of Ibuprofen and Paracetamol in tablet. HPLC methods are reported, the individual and in combination for estimation of Paracetamol and Ibuprofen in the tablet^[4-21].

Experimental

Apparatus:

A double beam UV-visible Spectrophotometer (Shimadzu, UV-1700, Japan), attached to a computer software UV probe 2.0, with a spectral width of 2 nm, wavelength accuracy of 0.5 nm and pair of 1 cm matched quartz cells, Analytical balance (Shimadzu), Ultrasonicator (Frontline FS 4 Mumbai, India), Corning volumetric flasks and pipettes of borosilicate glass were used for the development of proposed method.

Reagents and Solutions:

Pure Ibuprofen and Paracetamol and its pharmaceuticals formulation were kindly gifted from Gujarat Liqui pharmacaps Limited, Waghodia, Baroda. All the chemicals and reagents were of A.R grade and purchased from Merck Ltd, Mumbai.

Procedure for Calibration Curve:

Standard solutions of Ibuprofen in the concentration range of 4 µg/mL to 14 µg/mL obtained by transferring (0.4, 0.6, 0.8, 1.0, 1.2, 1.4 mL) of Ibuprofen stock solution (100 µg/mL) to the series of 10 mL volumetric flasks and standard solutions of Paracetamol in the concentration range of 2 µg/mL to 12 µg/mL were obtained by transferring (0.2, 0.4, 0.6, 0.8, 1.0, 1.2 mL) of Paracetamol stock solution (100 µg/mL) to the series of 10 mL volumetric flasks. Then methanol was added to each volumetric flask up to 10 mL. All dilutions were scanned in wavelength range of 200 nm to 400 nm. The absorbances were plotted against the respective concentrations to obtain the calibration curves. A representative overlain spectrum of Ibuprofen and Paracetamol in methanol is shown in Fig 1.

Formation of Simultaneous Equation:

Set of two simultaneous equations were:

$$C_x = (A_2 a_{y1} - A_1 a_{y2}) / (a_{x2} a_{y1} - a_{x1} a_{y2}) \text{ and}$$

$$C_y = (A_1 a_{x2} - A_2 a_{x1}) / (a_{x2} a_{y1} - a_{x1} a_{y2}),$$

Where A_1 and A_2 are the absorbance of sample solutions at 224.0 nm and 248.0 nm respectively. C_x and C_y are concentration of Ibuprofen and Paracetamol in mg/mL in sample solution. By substituting the values of A_1 and A_2 the values of C_x and C_y can be calculated by solving the two equations simultaneously. Here, a_{x1} and a_{x2} are the absorptivity coefficient of Ibuprofen at 224.0 nm and 248.0 nm respectively; a_{y1} and a_{y2} are the absorptivity coefficient of Paracetamol at 224.0 nm and 248.0 nm respectively. The optical parameters & regression characteristic for Ibuprofen and Paracetamol are shown in Table 1.

Method Validation

The linearity range for Ibuprofen and Paracetamol were 4-14 µg/mL and 2-12 µg/mL respectively. Recovery studies was carried out by addition of standard drug solution to pre-analysed soft gelatin capsule sample solution at three different concentration levels taking into consideration percentage purity of added bulk drug sample. The results of the recovery studies are found to be

satisfactory and shown in Table 2. The results obtained from recovery study (accuracy study) indicated that mean of percentage recovery were 99.70 ± 1.08 and 100.16 ± 1.02 for Ibuprofen and Paracetamol, respectively. Repeatability studies were found to be satisfactory with % RSD 1.44 and 0.95 for Ibuprofen and Paracetamol, respectively. Interday studies showed % RSD 0.25-0.89 and 0.25-0.76 for Ibuprofen and Paracetamol, respectively. Intraday studies showed % RSD 0.29-0.45 and 0.39-1.02 for Ibuprofen and Paracetamol, respectively. The results of Intra and Inter day studies are shown in Table 3. The limit of detection (LOD) was calculated to be 0.36 µg/mL and 0.28 µg/mL for Ibuprofen and paracetamol, respectively. The limit of quantification (LOQ) was calculated to be 1.08 µg/mL and 0.84 µg/mL for Ibuprofen and Paracetamol, respectively.

Estimation of Ibuprofen and Paracetamol in Pharmaceutical soft gelatin capsule Dosage form:

Mix content of 20 soft gelatin capsule and calculate the average content weight of one capsule. Take average content weight of one capsule. Add 80 mL of methanol; heat it for 25 minutes at 50-55 °C. Filter this solution and make up the volume of filtrate with methanol up to 100 mL. i.e., it contains 400 mg/100 mL of ibuprofen and 325 mg/100 mL of paracetamol, this solution was appropriately diluted to get approximate concentration of 6 µg/mL of ibuprofen and 5 µg/mL of paracetamol. The absorbance of sample solution was measured at 224.0 nm and 248.0 nm against blank. The content of Ibuprofen and Paracetamol in soft gelatin capsule was calculated using two framed simultaneous equations and results of analysis are shown in Table 4.

Results and Discussion

The proposed methods for simultaneous estimation of Ibuprofen and Paracetamol in combined dosage form were found to be simple, rapid, accurate, precise, specific and economical. Since HPLC method is reported for simultaneous analysis of the two drugs earlier, the developed method can be used for routine analysis of two drugs in combined dosage forms. The method involving formation and solving of simultaneous equation is very simple for routine analysis of two drugs in combined dosage forms. Once the equations are formed, then only measurement of the absorbance of sample solution at two wavelengths and simple calculations are required.

Table 1: Optical parameters & regression characteristic for Ibuprofen and Paracetamol

Parameters	Ibuprofen		Paracetamol	
	Wavelength (nm)	224.0	248.0	224.0
Beer's Law limit ($\mu\text{g}/\text{mL}$)	4-14	4-14	2-12	2-12
Sandell's sensitivity ($\mu\text{g}/\text{cm}^2/0.001$ absorbance unit)	2.43×10^{-2}	2.73×10^{-2}	2.76×10^{-2}	1.12×10^{-2}
Regression equation(*Y)	$Y=0.0376x + 0.113$	$Y=0.0617x + 0.0107$	$Y=0.0948x + 0.006$	$Y= 0.0887x + 0.0033$
Slop (m)	0.0376	0.0617	0.0948	0.0887
Intercept (c)	0.113	0.0107	0.006	0.003
Correlation coefficient (r^2)	0.9993	0.9996	0.9998	0.9997

Table 2: Results of recovery studies

Drug	Conc. added (mcg/mL)	% Conc. recovered	Mean Recovery \pm SD
Ibuprofen	4	99.96 ± 0.82	99.70 ± 1.08
	6	100.25 ± 1.14	
	8	98.89 ± 1.30	
Paracetamol	4	98.88 ± 0.78	100.16 ± 1.02
	6	101.24 ± 0.64	
	8	100.36 ± 1.64	

*Average of three determinations

Table 3: Inter-day and Intra-day precision

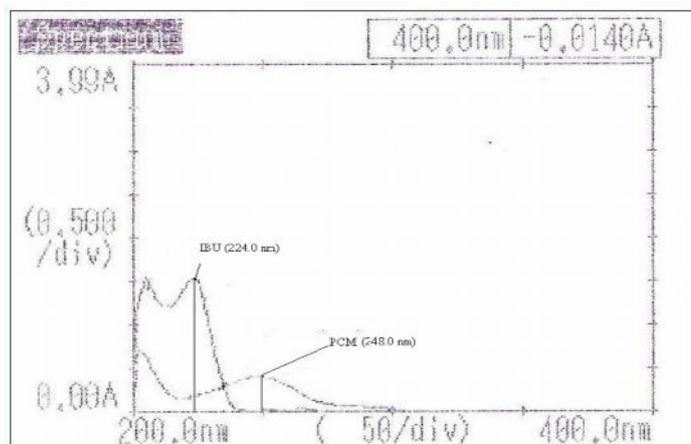
Inter-day						Intra-day					
Amount taken*		Amount found**		%RSD		Amount taken		Amount found**		%RSD	
IBU	PCM	IBU	PCM	IBU	PCM	IBU	PCM	IBU	PCM	IBU	PCM
4	4	3.99	3.91	0.25	0.26	4	4	3.95	3.90	0.29	0.39
6	6	6.02	5.99	0.28	0.76	6	6	5.97	5.92	0.31	1.02
8	8	7.96	8.04	0.89	0.25	8	8	7.94	8.01	0.45	0.84

*Concentration in μg

** Average of three determinations

Table 4: Results of analysis of soft gelatin capsule

Formulation	Label claim ^a		Amount Found		%Recovery \pm SD ^b	
	IBU	PCM	IBU	PCM	IBU	PCM
soft gelatin capsule	400	325	396.24	323.78	99.06 ± 0.12	99.62 ± 0.49

Fig.1: Overlain spectra of Ibuprofen and Paracetamol

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