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Development and Validation of UV Spectrophotometric Method for Simultaneous Estimation of Ibuprofen, Paracetamol and Caffeine in Pharmaceutical Dosage Form

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ABSTRACT

A simple, sensitive, accurate and precise simultaneous UV spectrophotometric method has been developed for the estimation of Ibuprofen, Paracetamol and Caffeine in tablet dosage form. The absorption maxima of the drugs were found to be 223, 248 and 272 nm for Ibuprofen, Paracetamol and Caffeine respectively, in methanol, using a Shimadzu UV–Visible spectrophotometer (model UV-1800). Ibuprofen, Paracetamol and Caffeine obeyed Beer's law in the concentration range of 10-70 µg ml^{-1}, 10-60 µg ml^{-1} and 10-70 µg ml^{-1} respectively. The correlation coefficient was found to be 0.999, 0.999, and 0.999 for Ibuprofen, Paracetamol and Caffeine respectively. The method was validated for various parameters according to ICH guidelines. The low relative standard deviation values indicate good precision and high recovery values indicate accuracy of the proposed method. Assay results were in good agreement with label claim.

Keywords: Ibuprofen, Paracetamol, Caffeine, UV spectrophotometric method, simultaneous equation method.

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INTRODUCTION

Ibuprofen (IBU), chemically 2-[4-(2-methylpropyl) phenyl]propanoic acid (Figure 1), is an Anti-Inflammatory agent. Its pharmacological effects are believed to be due to inhibition of cyclooxygenase-2 (COX-2) which decreases the synthesis of prostaglandins involved in mediating inflammation, pain, fever and swelling[1]. Paracetamol (PAR) chemically is N-(4-hydroxyphenyl)acetamide (Figure 2). It is an Analgesic and Antipyretic agent. It act primarily in the CNS, increasing the pain threshold by inhibiting both isoforms of cyclooxygenase, COX-1, COX-2, and COX-3 enzymes involved in prostaglandin synthesis. The antipyretic properties of Paracetamol are likely due to direct effects on the heat-regulating centres of the hypothalamus resulting in peripheral vasodilation, sweating and hence heat dissipation[2]. Caffeine (CAF) chemically is 1, 3, 7-trimethyl-2, 3, 6, 7-tetrahydro-1H-purine-2,6-dione (Figure 3). It is a central nervous system stimulant. It acts by inhibition of cyclic nucleotide phosphodiesterases, antagonism of adenosine receptors, and modulation of intracellular calcium handling[3].

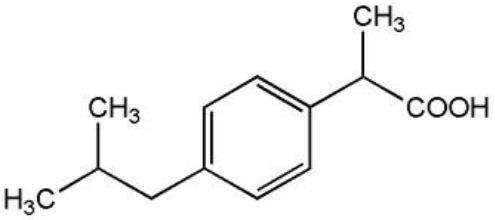

Figure 1. Ibuprofen

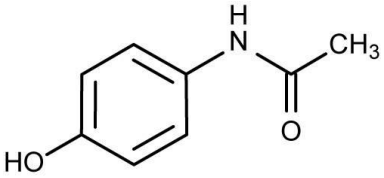

Figure 2. Paracetamol

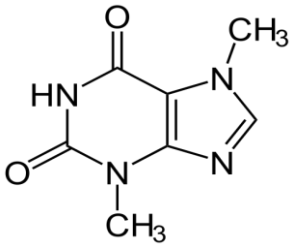

Figure 3. Caffeine

The combination of Ibuprofen, Paracetamol and Caffeine is prescribed by physician for the treatment of pain, fever and inflammation associated with musculoskeletal and joint disorders. Literature survey reveals several methods that have been used for the quantitative determination of these three drugs individually and in combination with other drugs[4-9]. The objective of the work is to develop a new UV spectrophotometric method for the simultaneous estimation of Ibuprofen, Paracetamol and Caffeine in pharmaceutical dosage form.

MATERIALS AND METHOD

Chemicals: Methanol, ethanol, and distilled water.

Drugs: Ibuprofen, Paracetamol and Caffeine pure powder were gift samples supplied from Intaas Pharmaceutical Limited, India. Formulation, Norflam plus (Label claim: IBU 400 mg, PAR 325 mg and CAF 30 mg) was manufactured by Brussels Laboratories Pvt. Ltd. and purchased from local pharmacy in Hyderabad, India.

Instrument: Shimadzu UV–Visible spectrophotometer (model UV-1800) was employed with a spectral band width of 1 nm and a wavelength accuracy of 0.3 nm (with automatic wavelength correction with a pair of 1 cm matched quartz cells).

METHOD:

Selection of solvent and wavelength:

Solubility of IBU, PAR and CAF was checked in solvents like ethanol, water and methanol. UV spectrum of the three drugs in these solutions were recorded. The absorbance of the three drugs was found maximum in methanol solvent compared to other solvents and three wavelengths 223, 248 and 272 nm (Figure 4) were selected which are the λmax of IBU, PAR and CAF respectively.

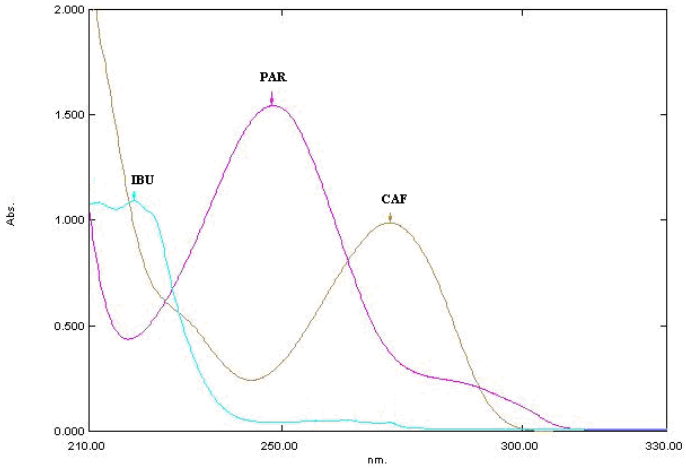

Figure 4. Overlay spectra of Ibuprofen, Paracetamol and Caffeine showing selected wavelength

Preparation Standard Stock Solutions:

IBU, PAR and CAF (10 mg each) were separately weighed and transferred to 100 ml volumetric flask and all the three drugs were dissolved in methanol to get a concentration of 100 µg ml^{-1}.

Application of Simultaneous equation method[10]:

In quantitative estimation of three components by Simultaneous equation method, three wavelengths i.e., 223 nm of IBU, 248 nm of PAR and 272 nm of CAF were selected as their respective λmax from the overlain spectrum, at which three drugs have maximum absorbance. The concentrations of three drugs in the mixture can be calculated using the following equations.

$$C_{IBU} = \frac{(A1\ (ay2az3-az2ay3) - ay1\ (A2az3-az2A3) + az1\ (A2ay3-ay2A3)}{ax1(ay2az3-az2ay3) - ay1(ax2az3-az2ax3) + az1(ax2ay3-ay2ax3)}$$

$$C_{PAR} = \frac{(ax1(A2az3-az2A3) - A1(ax2az3-az2ax3) + az1(ax2A3-A2ax3)}{ax1\ (ay2az3-az2ay3) - ay1\ (ax2az3-az2ax3) + az1\ (ax2ay3-ay2ax3)}$$

$$C_{CAF} = \frac{(ax1(ay2A3-A2ay3) - ay1(ax2A3-A2ax3) + A1(ax2ay3-ay2ax3)}{ax1\ (ay2az3-az2ay3) - ay1\ (ax2az3-az2ax3) + az1(ax2ay3-ay2ax3)}$$

Where, $C_{IBU,}$ C_{PAR} and C_{CAF} are the concentrations of IBU, PAR and CAF respectively in mixture and in sample solutions. A_1, A_2 and A_3 are the absorbances of sample at 223, 248 and 272 nm, respectively, ax_1, ax_2 and ax_3 are the absorptivity of IBU at 223, 248 and 272 nm respectively, ay_1, ay_2 and ay_3 are the absorptivity of PAR at 223, 248 and 272 nm, respectively, az_1, az_2 and az_3 are the absorptivity of CAF at 223, 248 and 272 nm, respectively.

Analysis of marketed formulation:

For the analysis, 20 tablets were weighed and their average weight was determined. The tablets were then crushed to fine powder and powder equivalent to weight of one tablet was transferred to 100 ml volumetric flask and dissolved in 50 ml of methanol for 10 min with vigorous shaking. Finally, the volume was made up to the mark with methanol. The solution was then filtered through whatmann filter paper. From this solution, 1 ml was pipette out into a 10 ml volumetric flask and diluted with methanol up to the mark. From this solution, 0.4 ml was transferred into a 10 ml volumetric flask and diluted with methanol up to the mark. The absorbance of the above solution was measured at 223, 248 and 272 nm. The concentration of each analyte was determined using the simultaneous equation.

RESULTS AND DISCUSSION:

The analytical method was validated with respect to parameters such as linearity, precision, limit of detection (LOD), limit of quantitation (LOQ) and accuracy.

Linearity:

Calibration graph was found to be linear that is adherence to the system of Beer's law which was found over the concentration range of 10-70 µg ml^{-1} for IBU, 10-60 µg ml^{-1} for PAR and 10-70 µg ml^{-1} for CAF (Figure 5-7). Absorbance and concentration was subjected to least square linear regression analysis to calculate the calibration equation and correlation coefficients. The regression data as given in Table 1, showed a good linear relationship.

Table 1: Linearity

Parameter	Ibuprofen	Paracetamol	Caffeine
Linearity range	10-70 µg ml^{-1}	10-60 µg ml^{-1}	10-70 µg ml^{-1}
Correlation coefficient	0.999	0.999	0.999
Slope	0.041	0.065	0.047
Intercept	0.025	0.044	0.019

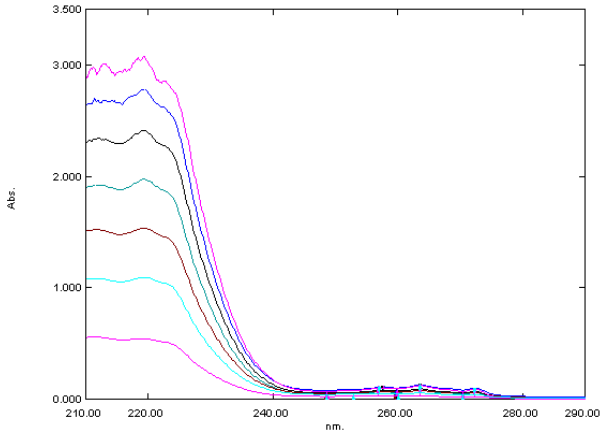

Figure 5. Overlay spectra of Standard Ibuprofen (10-70 µg ml^{-1})

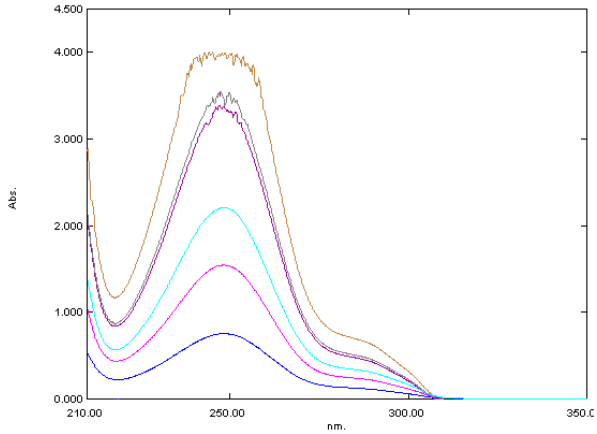

Figure 6. Overlay spectra of Standard Paracetamol (10-60 µg ml^{-1})

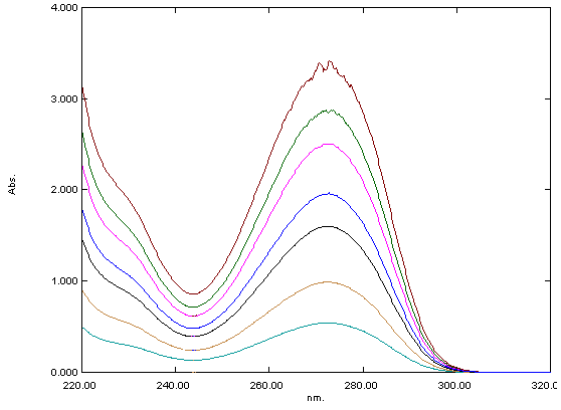

Figure 7. Overlay spectra of Standard Caffeine (10-70 µg ml^{-1})

Precision:

To check the degree of repeatability of the method, suitable statistical evaluation was carried out. The concentrations of three drugs were 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 found to be less than 2. The results were shown in Table 2.

Table 2: Precision studies

Drug	Concentration (µg ml^{-1})	Intraday precision % *RSD	Interday precision % *RSD
Ibuprofen	20	0.241	0.314
Paracetamol	20	0.173	0.287
Caffeine	20	0.275	0.362

***** mean of six observations

LOD and LOQ:

LOD and LOQ was found to be 0.64 µg ml^{-1} and 2.1 µg ml^{-1} for IBU, 0.62 µg ml^{-1} and 1.09 µg ml^{-1} for PAR, 0.87 µg ml^{-1} and 1.15 µg ml^{-1} for CAF respectively.

Accuracy:

To check the accuracy of the developed method and to study the interference of formulation additives, analytical recovery experiments were carried out by the standard addition method. The recovery studies were carried out at three different levels i.e. 50%, 100% and 150% level. The percentage recovery values were shown in Table 3.

Table 3: Accuracy

Drug	% Recovery			% *RSD		
	50% level	100% level	150% level	50% level	100% level	150% Level
Ibuprofen	99.71	100.07	100.11	0.382	0.461	0.218
Paracetamol	99.58	99.75	100.08	0.532	0.498	0.253
Caffeine	99.52	100.03	100.66	0.288	0.319	0.427

***** mean of six observations

Analysis of formulation:

The amount of each drug present in formulation was calculated using the simultaneous equation. The spectrum of formulation sample is shown in Figure 8. The results were shown in Table 4.

Table 4: Analysis of formulation

Drug	Labeled amount (mg/tablet)	Amount estimated (mg/tablet)	% Label claim	% *RSD
Ibuprofen	400	400.13	100.03	0.423
Paracetamol	325	324.42	99.82	0.472
Caffeine	30	29.84	99.46	0.348

***** mean of six observations

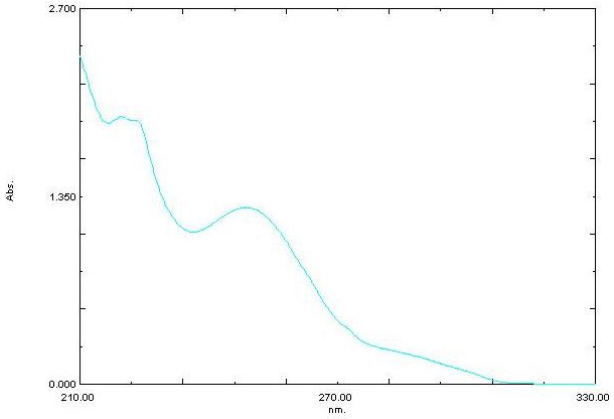

Figure 8. Spectrum of formulation containing Ibuprofen, Paracetamol and Caffeine

CONCLUSION:

The developed UV spectrophotometric method is simple, precise, accurate, linear, reproducible and repeatable for the estimation of IBU, PAR and CAF in pharmaceutical dosage forms without any interference from the excipients. It can be successfully applied for the routine analysis of all the three drugs in pharmaceutical dosage forms.

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