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SHORT COMMUNICATION

Simultaneous Equation Method for Simultaneous Estimation of Paracetamol and Ibuprofen in Combined Dosage Form.

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ABSTRACT

A simple reproducible simultaneous equation method, requiring no prior separation, has been developed for the estimation of ibuprofen and paracetamol in combined dosage form. Ibuprofen has absorbance maxima at 220 nm and paracetamol at 248.40 nm using ethanol as solvent. The method obeys Beer's Law in concentration ranges employed for the estimation. The results of the analysis were validated statistically and recovery studies were carried out as per ICH guidelines. Also the developed method was successfully employed for dissolution studies in tablet dosage form.

Key Words: Paracetamol, Ibuprofen, Simultaneous equation, Validation.

INTRODUCTION

The relief of pain has been described as a universal human right but is not always easily achieved [1]. Opioid analgesics are effective, but have troublesome and potentially dangerous side-effects, and their potential for abuse may lead to regulatory and logistical difficulties. Non-steroidal anti-inflammatory drugs (NSAIDs) have fewer regulatory restrictions, but they too have important adverse effects which are more likely at higher dose or with longer courses [2]. Paracetamol is widely used and is very safe at the recommended dose of 4 g per day, [3] but does not always provide adequate pain relief on its own. Combining analgesics offers the possibility of increasing effectiveness without increasing dose (and therefore risk) [4, 5]. Prescribing paracetamol and ibuprofen together is common in clinical practice.[6 – 8]

Paracetamol is chemically N-(4-hydroxyphenyl) acetamide. Ibuprofen is chemically 2[4-(2-methyl propyl) phenyl] propanoic acid. Literature survey reveals that spectrophotometry [9], TLC [10], HPTLC [11], and LC-MS [12] are available for the determination of paracetamol and spectrophotometric [13], chromatography [14] and electrochemical [15] method for the determination of ibuprofen. Also various methods like multivariate calibration [16], HPLC [17], Reverse phase HPLC [18], derivative spectrophotometry [19] method have been described in literature for the determination of paracetamol and ibuprofen in pharmaceutical preparations.

The review of the literature revealed that no simultaneous equation method is yet reported for the simultaneous estimation of both the drugs in combined dosage forms. This paper describes simple, rapid, accurate, reproducible and economical method for the simultaneous estimation of ibuprofen and paracetamol in tablet formulations using simultaneous equation method.

MATERIALS & METHODS

Instrument, reagents and chemicals

A Shimadzu UV/Visible spectrophotometer, model No.UV-1800 was employed with spectral band width of 2 nm and wavelength accuracy of ± 0.1 nm, with automatic wavelength correction employing a pair of quartz cells. A Denver electronic analytical balance (TB-214) was used for weighing the sample. Pure drug sample of ibuprofen and paracetamol were procured from Dr. Reddy's Ltd., Hyderabad. Tablet formulation containing Ibuprofen (400mg) and paracetamol (325 mg) was procured from local market. Ethanol was used as solvent.

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EXPERIMENTAL

According to the solubility characteristics of drug Ethanol was selected as solvent for analysis.

Standard stock solutions having 100µg/ml of Ibuprofen and paracetamol were prepared by dissolving separately 10 mg of each drug in 100 ml ethanol. The stock solutions were individually diluted to get final concentration of 20 µg/ml each and the diluted solutions were scanned in 200-400 nm range to determine the maximum absorbance(λmax). Ibuprofen and paracetamol have λmax at 220 nm and 248.40 nm, respectively [**Fig 1**].

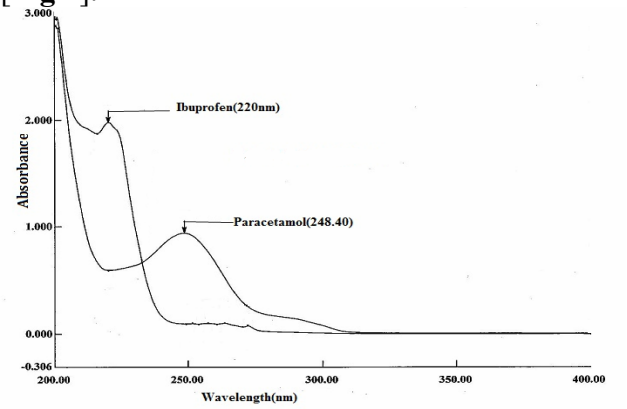

Fig. 1 Overlain spectra of Ibuprofen (IBP) and Paracetamol (PCM).

Different aliquots were taken from stock solutions and diluted to prepare series of concentrations. Calibration curves were found to linear in the concentration range 1-10 µg/ml for both the drug. Coefficient of correlation was found to be 0.9982 for ibuprofen calibration curve and 0.9981 for paracetamol calibration curve.

Simultaneous equation method

The absorptivity values of the drugs were determined at λmax of PCM and IBP. The absorptivity value of the drugs is the ratio of absorbance at selected wavelengths with the concentration of drugs in mg/ml. A set of two simultaneous equations were framed using these absorptivity values.

$A_1 = ax_1C_{PCM} + ax_2C_{IBP}$ (1)

$A_2 = ay_1C_{PCM} + ay_2C_{IBP}$ (2)

Where, A_1 and A_2 are the absorbance of the tablet sample solution at 248.40 nm and 220 nm respectively. $ax_1$and $ay_1$are absorptivities of PCM at 248.40 nm and 220 nm respectively. $ax_2$and ay_2 are absorptivities of IBP at 248.40 nm and 220 nm respectively. C_{PCM} is the concentration of PCM and C_{IBP} is the concentration of IBP in mg/ml.

By applying the cramer's rule to equation 1 and 2, the concentration C_{PCM} and C_{IBP} can be obtained as follows.

$$C_{IBP} = \frac{ax_1A_2 - ay_1A_1}{ax_1ay_2 - ay_1ax_2} \quad (3)$$

$$C_{PCM} = \frac{ay_2A_1 - ax_2A_2}{ax_1ay_2 - ay_1ax_2} \quad (4)$$

Assay of tablet formulation by simultaneous equation method

20 tablets were weight, crushed to fine powder and the content of 20 tablets was transferred to 100ml volumetric flask, dissolved in 30 ml ethanol and sonicated for 10 Min. The volume was then made up to the mark using same solvent. The resulting solution was filtered through whatman filter paper and from filtrate 5 ml was taken which was equivalent to average weight of one tablet i.e., it contain 400 mg/5ml of IBP and 325 mg/5ml of PCM, this solution was appropriately diluted to get approximate concentration of 8 µg/ml of IBP and 6.5 µg/ml of PCM .

Absorbances of sample solutions were recorded at 248.40 nm and 220 nm and the concentration of two drugs in the sample were determined by using equation 3 and 4(simultaneous equation method).

The results of estimation of both these drugs by using simultaneous equation method are shown in **Table 1.**

Table 1: Analysis of tablet formulation

Method	Tablet Sample	Label claim (mg/tablet)		% Label claim found*		±Standard deviation		Relative standard deviation	
		PCM	IBP	PCM	IBP	PCM	IBP	PCM	IBP
Simultaneous equation method	T_1	325	400	99.33	98.59	0.4239	0.6439	0.4268	0.6532
	T_2	325	400	99.3	99.11	0.3668	0.6218	0.3694	0.6273

*Average of six estimations.

To ascertain the accuracy of the proposed method, recovery studies were carried out by standard addition method at three different levels (80, 100, 120% of final concentration). A known amount of PCM and IBP pure drugs were added to preanalysed tablet powder and the samples were

then analysed by proposed method. Percent recovery was calculated by following formula: % recovery = $\frac{(T-A)}{S}\times 100$. Where T is the total amount of drug estimated. A is the amount of drug contributed by tablet powder (Estimated by proposed methods), S is the amount of pure drug added to the preanalysed tablet powder. Results of recovery studies are presented in **Table 2.**

Table 2: Results of recovery studies

Label of recovery	Drugs	Amount of drug Added µg/ml	Simultaneous equation method		
			Recovery (%)*	±SD	Relative Standard Deviation
80%	PCM	5.2	99.45	0.2972	0.2989
	IBP	6.4	100.32	0.1497	0.1492
100%	PCM	6.5	99.26	0.3788	0.3186
	IBP	8	99.35	0.2171	0.2185
120%	PCM	7.8	100.36	0.2153	0.2145
	IBP	9.6	100.24	0.331	0.3323

*Mean of six estimations.

RESULT & DISCUSSION

The solubility of PCM and IBP was studied and ethanol(99.9%) was selected as a choice of solvent. PCM and IBP showed well defined λmax at 248.40 nm and 220 nm respectively. The wavelengths 248.40 nm and 220 nm were considered for development of simultaneous equation method. The two drugs invidually and in their mixture were found to follow Beer-Lambert's law over the concentration range of 1-10 µg/ml for both PCM and IBP.

The methods were validated with respect to accuracy, precision, linearity and ruggedness. Accuracy of the proposed method was ascertained on the basis of recovery studies (Table 2) performed by standard addition method. The recoveries of both the drugs were observed to be very close to 100% representing the accuracy of the method and also show that excipients have no interference in the estimation.

The standard deviation and relative standard deviation (RSD) calculated for both the methods are low, indicating high degree of precision of the methods. The RSD is also less than 2% as required by ICH guidelines. Recovery studies were performed at three different levels i.e. 80, 100, 120 % of the final concentration of marketed analysis sample. The results were found to linear in the concentration range under study (linearity and range).

CONCLUSION

The proposed method was found to be simple, accurate, economical, and rapid for routine simultaneous estimation of two drugs. The values of standard deviation and coefficient of variation were satisfactorily low and recoveries studies indicate the reproducibility and accuracy of the method.

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