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Spectrophotometric Simultaneous Determination of Ibuprofen and Paracetamol in Tablet Dosage Form

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Abstract: *The aim of the study to describe a simple, precise, sensitive, rapid, accurate and economical simultaneous equation method for the determination of Ibuprofen and Paracetamol in tablet dosage form. The method involved solving simultaneous equations based on measurement of absorbance at two wavelengths 224nm and 249nm. The proposed method was validated for linearity, accuracy and precision. The linearity was obtained in the concentration range 20 - 60µg/mL for Ibuprofen and 16.25 – 48.75µg/mL for Diclofenac sodium. The percentage recovery was found to be 99 - 101% for Ibuprofen and 99 – 101% for Paracetamol indicates that the method was accurate and precise for simultaneous estimation of Chlorzoxazone and Diclofenac sodium in tablets.*

Keywords: Simultaneous equation method, Ibuprofen and Paracetamol

I. INTRODUCTION

The 2-arylproprionic acid derivative, Ibuprofen [RS-2- (4-isobutyl-phenyl)propionic acid], is one of the mostpotent 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. 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 Enantiomers, even if it is known that the pharmacological activity is due almost exclusively to the S- enantiomer[Fig 1].

Paracetamol (PCT) is chemically N (4- hydroxyl phenyl) acetamide and is used as analgesic and anti-pyretic agent. It is well known analgesic drug which is very effective to the treatment for relief pain and fever in adults and children. It has molecular formula $C_8H_9NO_2$ and molecular weight 151.16. It has a narrow therapeutic index- the therapeutic dose is close to the toxic dose. [Fig 2]

Literature survey revealed[1 – 9] that various methods reported for the analysis of Ibuprofen and Paracetamol in pharmaceuticals viz, UV spectrophotometry, reverse phase HPLC stability indicating, visible spectrophotometry, HPTLC. Aim of present work was to develop simple, economical, rapid, precise and accurate method for simultaneous determination of Ibuprofen and Paracetamol. The key advantage of developed UV spectrophotometry method is that several samples can be analyzed using simultaneous equation method. The proposed method was validated as per ICH guidelines and its updated international convention.

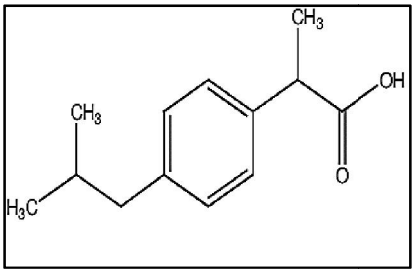

Figure 1 Structure of Ibuprofen

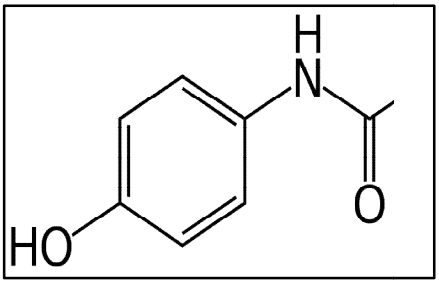

Figure 2: Structure of Paracetamol

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II. EXPERIMENTAL

Chemicals and reagents:

Methanol Analytical grade was procured from Merck India Limited, Mumbai. Water HPLC grade was obtained from Merck Specialties Private Limited, Mumbai. Reference standards of Ibuprofen and paracetamol were gifted samples.

Standard stock preparation:

Preparation of standard drug solution:

40mg of ibuprofen and 32.5 mg of Paracetamol was separately weighed and transferred to a 50cm^3 volumetric flask. It was dissolved in a minimum quantity of methanol and then diluted up to the mark with methanol. The concentration of the solution obtained was 800µg/mL for Ibuprofen and 650 µg/mL for Paracetamol. 10cm^3 of each of this solutionwas diluted to 100 cm^3 in a volumetric flask with methanol. The concentration of the solution obtained was 80µg/mL for Ibuprofen and 65µg/mL for Paracetamol.

Preparation of sample solution:

Twenty tablets were weighed and average weight was calculated. These tablets were powdered and 0.0820gm of powdered tablet was taken in a 100 mL volumetric flask, 10mL of methanol was added and sonicated for 20minutes and shaken by mechanical means for 20minutes at 250rpm. Further the solution was diluted with methanol. The solution was mixed and allows settled for 5 minutes. The solution was filtered through Whatman filter paper No 41. Then 10 mL of the filtrate was diluted to 100mL with diluents and mixed. The concentrations obtained were 40 µg/mL of Ibuprofen and 32.5 µg/mL of Paracetamol. This sample solution was used for further determination.

METHOD IN BRIEF:

The present work describes an ultraviolet spectrophotometric method for the quantitative simultaneous determination of Ibuprofen and Paracetamol from its bulk drug and pharmaceutical preparation. Ibuprofen and Paracetamol absorb the radiation in the ultraviolet region. The Proposed ultraviolet spectrophotometric method is based on the measurement of absorbed ultraviolet radiations by both the analytes. The absorbance measurement was carried out at the λ_{max} of Ibuprofen and Paracetamol. Paracetamol shows maximum absorbance at 249nm wavelength while Ibuprofen shows at 224nm. The molar absorptivities of both the analytes were found at their respective λmax value. Using the molar absorptivities of both the analytes simultaneous equation was constructed and the concentration of analytes was determined. The proposed ultraviolet spectrophotometric method was subjected to statistical validation to determine its accuracy and precision.

OPTIMIZATION OF EXPERIMENTAL CONDITIONS:

The instrument used for the analysis of the samples is LAMBDA 25 UV/Visible Spectrophotometer, Range: 190 nm - 1100 nm, Bandwidth: 1 nm.The solvents that are commonly used in spectrophotometric analysis are water, dilute bases and organic solvents. Most of the drugs are soluble in organic solvents like methanol, acetonitrile etc. In the present study the drugs used are Ibuprofen and Paracetamol. Both the drugs are highly soluble in methanol. Other solvents were also tried but methanol gives higher $E_{1\%}$ Value.

Table 1 $E_{1\%}$ Value for Ibuprofen and Paracetamol

Solvent	Ibuprofen		Paracetamol	
	Conc. in µg/mL	**$E_{1\%}$**	Conc. in µg/mL	**$E_{1\%}$**
Methanol	40	**919.2**	32.5	**850**

From the above $E_{1\%}$ value data it has been found that methanol was chosen as a solvent for the preparation of solution as it gives higher $E_{1\%}$ value.

Method Validation:

The method was validated as per ICH guidelines [10] for specificity, linearity, quantification limit, precision, accuracy, recovery and stability. Specificity was investigated by analyzing the blank diluents and samples of 100% level for any interference of the endogenous material at the absorbance of Ibuprofen and Paracetamol. The linearity of the method

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was tested by taking several aliquots of standard solutions of Ibuprofen and Paracetamol in 50mL volumetric flask and diluted upto the mark with solvent. The final concentration of Ibuprofen and Paracetamol was 20 - 60 µg/mL and 16.25 – 48.75 µg/mL respectively.

The accuracy of the method was determined by recovery experiments. A standard addition method was employed for this experiment. A known quantity of each drug substance (Ibuprofen and Paracetamol) corresponding to 0%, 10%, 20% and 30% of the label claim of each drug was added. The accuracy was expressed as a percentage of analytes recovered by the assay. In the present research work 40 ppm sample solution was considered as 100% (0 level).

As a part of method validation, Intermediate precision was performed by carrying out the same assay procedure on a different instrument on a different day under similar experimental conditions. Robustness of the proposed method was determined by minor changes in the λmax of both the analytes.

III. RESULTS AND DISCUSSIONS

To develop rapid, low cost and sensitive UV method for simultaneous determination of IBU&PCT the optimized conditions were necessary. A study of overlain spectra of Ibuprofen and Paracetamolin methanol shows that at 224nm Ibuprofen shows maximum absorbance whereas Paracetamol shows at 249nm. The overlain spectrum also shows that both the analytes show considerable absorbances at their λmax values. Hence it was possible to construct simultaneous equation.

$$Cx=\frac{A_2 0.0110 \; - A_1 \, 0.0217}{0.0100\times 0.0110 - \; 0.0226\times 0.0217}$$

$$\text{and } Cy \; =\frac{A_1\times 0.0100 \; - A_2\times 0.0226}{0.0100\times 0.0110 - \; 0.0226\times 0.0217}$$

The study of the system suitability test showed that the operating system has given good results and verified the reproducibility of the method.

Validation

Linearity:

Linearity of the method was tested from 50% to 150% of the targeted level of the assayconcentration (40µg/mL Ibuprofen and 32.5 µg/mL Paracetamol) for the two analytes. The standard solutions containing 20 – 60µg/mL Ibuprofen and 16.25 – 48.75 µg/mL Paracetamol were prepared from the standard stock solutions of Ibuprofen and Paracetamol. Linearity test solutions were analyzed in triplicate. The calibration graphs were plotted by using absorbance of the analytes against the concentration of the drug (in micrograms per milliliter). In the simultaneous determination, the calibration graphs were found to be linear for both the analytes in the mentioned concentration ranges. The regressionequations for Ibuprofen and Paracetamol. were found to be y = 0.081X + 0.143 and y = 0.0227X + 0.00120, and the correlation coefficients for the regression lines were 0.9994 and 0.9990, respectively.

Sensitivity:

Sandell's sensitivity of Ibuprofen and Paracetamol. was found to be sufficiently low.

Table 2 shows that very less amount of both the drugs can be effectively detected by this method.

Table 2: Sensitivity Parameters for Ibuprofen and Paracetamol.

Analyte	λ max (nm)	Molar absorptivity	Sandell's Sensitivity
Ibuprofen	224	3.280×10^3 lit.mol^{-1} cm^{-1}	0.04608 µg/cm^3/cm^2
Paracetamol	249	4.640×10^3 lit.mol^{-1} cm^{-1}	0.04444 µg/cm^3/cm^2

Recovery:

The accuracy of the method was determined by the standard addition method at three different levels. The sample solution of 100% level was considered as a zero level and 10%, 20% and 30% of the standard drug of analytes were

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added respectively. Each determination was performed in triplicates. The accuracy was then calculated as the percentage of the standard drug recovered by the recovery study. The recovery of Ibuprofen and Paracetamol from the standard mixture solution was found to be 99.13% -100.40% and 98.16-100.31%respectively. The recovery results show that Ibuprofen and Paracetamol could be quantified by this procedure simultaneously. The results are well within the acceptance limit and hence the method is accurate. Table 3 & 4 shows the % recoveries of Ibuprofen and Paracetamol.

Obs No	Levels in %	Absorbance		Initial amount in mg	Amt added in mg	Amt found in mg	% recovery
		at 224nm	at 249nm				
1	0%	0.95	0.54	40.0	0	40.115	100.29
2		0.954	0.545	40.0	0	39.980	99.95
3		0.953	0.537	40.0	0	39.995	99.99
1	10%	1.045	0.594	40.0	4.0	44.105	100.24
2		1.055	0.585	40.0	4.2	43.998	99.54
3		1.052	0.590	40.0	4.3	44.005	99.33
1	20%	1.140	0.648	40.0	8.0	48.102	100.21
2		1.448	0.645	40.0	8.2	48.210	100.02
3		1.441	0.645	40.0	8.1	48.115	100.03
1	30%	1.235	0.702	40.0	12.0	52.010	100.02
2		1.230	0.705	40.0	12.1	52.109	100.02
3		1.234	0.703	40.0	12.0	51.997	99.99
						Mean	99.97
						S.D	0.276
						%RSD	0.276
						Range of Recovery	99.33-100.24

Table 3 % recoveries of Ibuprofen

Obs No	Levels in %	Absorbance		Initial amount in mg	Amt added in mg	Amt found in mg	% recovery
		at 224nm	at 249nm				
1	0%	0.95	0.54	32.5	0	32.450	99.85
2		0.954	0.545	32.5	0	32.355	99.55
3		0.953	0.537	32.5	0	32.410	99.72
1	10%	1.045	0.594	32.5	3.25	35.751	100.00
2		1.055	0.585	32.5	3.30	35.659	99.75
3		1.052	0.590	32.5	3.28	35.750	100.00
1	20%	1.140	0.648	32.5	6.50	39.012	100.03
2		1.448	0.645	32.5	6.51	38.998	99.99
3		1.441	0.645	32.5	6.52	39.115	100.29
1	30%	1.235	0.702	32.5	9.75	42.250	100.00
2		1.230	0.705	32.5	9.77	42.152	99.77

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3		1.234	0.703	32.5	9.76	42.195	99.87
						Mean	99.90
						S.D	0.19
						%RSD	0.193
						Range of Recovery	99.55-100.29

Table 3 % recoveries of Paracetamol

Robustness:

Robustness study shows that the proposed method was found to be robustwhere minor variation in wavelength could not alter the assay of the analytes.

As a part of method validation, Intermediate precision was performed by carrying out the same assay procedure on a different instrument on a different day. The experimental conditions kept same.

Table 5: Cumulative % RSD of Ibuprofen & Paracetamol in precision and Intermediate precision

Obs No	Ibuprofen mg/tab	% LC Ibuprofen	Paracetamol mg/tab	% LC Paracetamol
M.P 1	400.15	100.04	325.05	100.02
M.P 2	399.82	99.96	325.1	100.03
M.P 3	399.94	99.99	325.18	100.06
M.P 4	400.50	100.13	324.98	99.99
M.P 5	400.23	100.06	324.85	99.95
M.P 6	400.16	100.04	325.54	100.17
I.P 1	400.15	100.04	325.62	100.19
I.P 2	399.68	99.92	324.81	99.94
I.P 3	399.96	99.99	324.69	99.90
I.P 4	398.98	99.75	325.48	100.15
I.P 5	400.09	100.02	325.23	100.07
I.P 6	399.42	99.86	325.02	100.01
Mean	399.92	99.98	325.13	100.04
S.D.	0.407	0.10	0.295	0.09
Cumulative % RSD	0.102	0.102	0.0909	0.091
Limits	NMT 2.00%		NMT 2.00%	

IV. CONCLUSION

The UV method has proved to be simple, specific, precise and accurate and is suitable for simultaneous determination of Ibuprofen and Paracetamol. The proposed method gives a good results among these analytes. High percentage of recovery shows that the method is accurate.

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