

Method Development and Validation for the Simultaneous Estimation of Paracetamol and Diclofenac by Green Spectroscopy in Tablet Dosage Form

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ABSTRACT

A simple, rapid, accurate, precise, and economic spectrophotometric method for simultaneous estimation of paracetamol and diclofenacin tablet dosage form have been developed and validated. Paracetamol and diclofenac show absorbance maximums at 242 and 276nm respectively by using 7.4 phosphate buffers, so absorbance was measured at the same wavelengths for the estimation of paracetamol and Diclofenac. Absorbance is measured at 240.2 nm (Isoabsorptive point) and 258.4nm (λ_{max} of diclofenac). Both drugs obey the Beer's Lambert's law in the concentration range of 10-30 μ g/mL. Methods are validated according to ICH guidelines and can be adopted for the routine analysis of Paracetamol and Diclofenac in tablet dosage form.

Keywords: Paracetamol, Diclofenac sodium, Simultaneous equation, Ethanol, UV Spectroscopy.

INTRODUCTION:

Paracetamol and Diclofenac are available in tablet dosage form. Chemically Paracetamol is *N*-(4-hydroxyphenyl) ethanamid, *N*-(4hydroxyphenyl) acetamide and its structure is shown in Fig.1. It has antipyretic and analgesic activity.

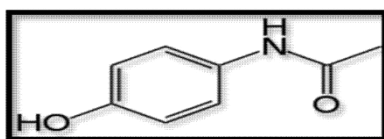


Fig.1:Structure of Paracetamol

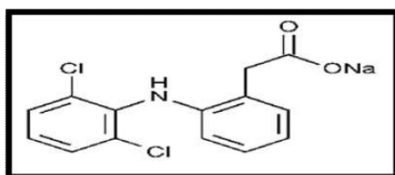


Fig.2: Structure of Diclofenac sodium

Diclofenac sodium is Sodium {2-[(2, 6-dichlorophenyl)amino]phenyl}acetate and its structure is as shown in Fig.2. It is widely used as an analgesic drug.

From the literature survey conducted, it was found that there are analytical methods reported for Paracetamol and Diclofenac Sodium either individually or in combination with other drugs by Simultaneous equation method and UV methods. There is no method reported for the estimation of Diclofenac Sodium and Paracetamol tablets in pharmaceutical dosage forms. So it was felt that there is a need to develop analytical methods for the estimation of Diclofenac Sodium and Paracetamol tablets.

MATERIALS AND METHODS

Instrumentation

1. Single pan balance.
2. Digital PHmeter
3. UV Double beam spectrophotometer 2800 (shimadzu), Path length 1 cm, UVRange: 200-400 nm, λ_{max} : 254 nm.

Reagents and Chemicals

Ethanol, Sodium Hydroxide, Hydrogen Chloride, Distilled Water

Reference Standard used: Diclofenac Sodium (%Purity: 99.93%) and Paracetamol (%Purity: 99.91%)

Determination of Maximum Wave Length (λ_{max}) for Paracetamol:

Preparation of stock solution:

Standard stock solution of paracetamol was prepared by dissolving accurately weighed 100 mg of paracetamol in 7.4 buffer solution in a 100 ml volumetric flask from this 1 ml is taken and dissolved in 100 ml buffer solution. The sample was then scanned in UV spectrophotometer from a range of 200–400 nm against buffer as blank and the wavelength corresponding to maximum absorbance in buffer was found at 242 nm.

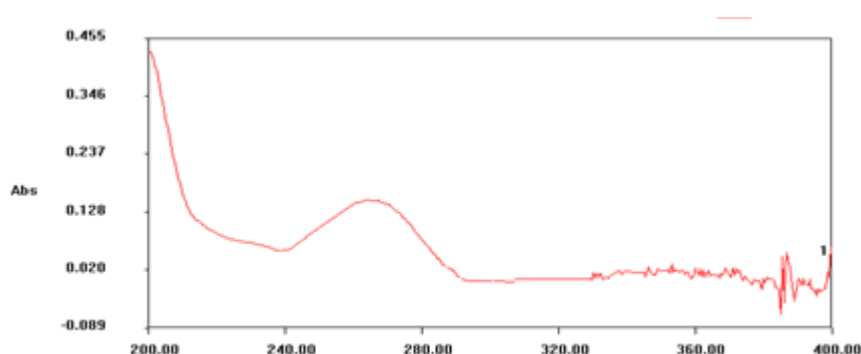


Fig.3: UV Spectrum of Paracetamol

Determination of Maximum Wave length (λ_{max}) for Diclofenac:

Preparation of stock solution:

Standard stock solution of diclofenac was prepared by dissolving accurately weighed 100 mg of diclofenac in 7.4 buffer solution in a 100 ml volumetric flask from this 1 ml is taken and dissolved in 100 ml buffer solution. The sample was then scanned in UV spectrophotometer from a range of 200–400 nm against buffer as blank and the wavelength corresponding to maximum absorbance in buffer was found at 276 nm.

Isobestic point for the Paracetamol and Diclofenac:

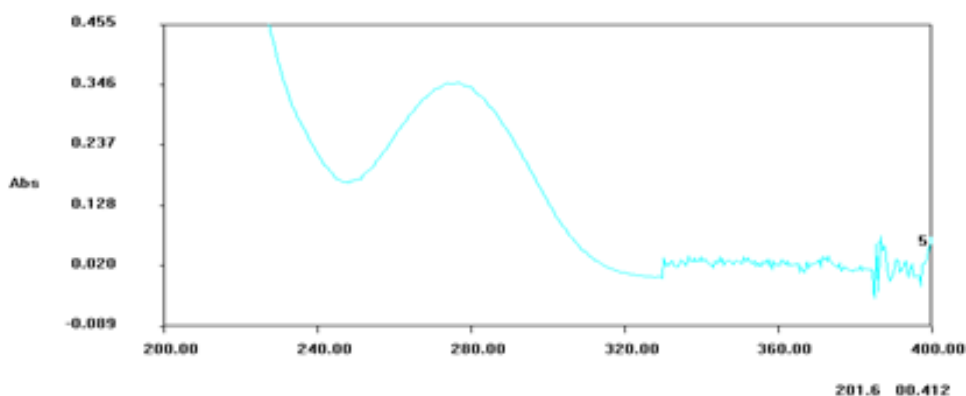


Fig.4: UV Spectrum of Diclofenac

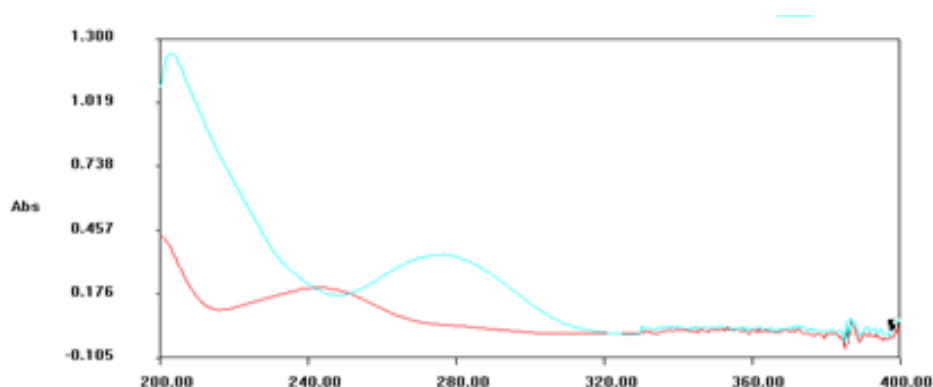


Fig.5: Overlaid UV Spectrum of Paracetamol and Diclofenac

Determination of maximum wavelength (λ_{max}) for Paracetamol and Diclofenac:

Preparation of sample solution- Sample stock solution of paracetamol and diclofenac was prepared by dissolving accurately weighed 132mg of paracetamol and diclofenac in 7.4 buffer solution in a 100ml volumetric flask from this 1ml is taken and dissolved in 100ml buffer solution. The samples were then scanned in UV spectrophotometer from a range of 200-400 nm against buffer as blank and the wavelength corresponding to maximum absorbance in buffer was found at 242nm and 276nm.

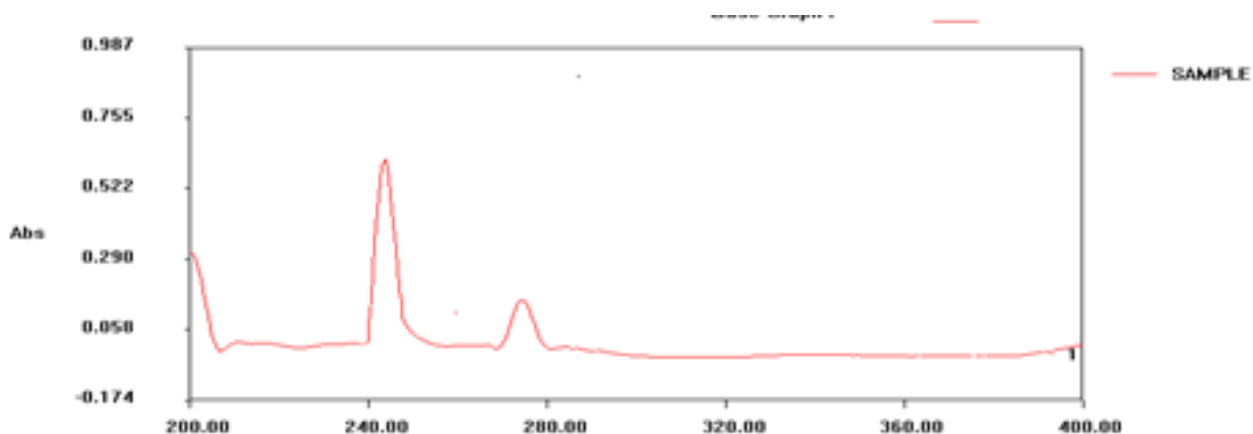


Fig.6: UV Spectrum of Paracetamol and Diclofenac Solution

Absorbance of paracetamol and diclofenac and its λ_{max} :

Wavelength	Paracetamol	Diclofenac	Sample	Absorbance of Paracetamol	Absorbance of Diclofenac
242	0.656	0.67	0.664	656	67
276	0.112	0.234	0.147	112	234

Simultaneous Equation Method:

$$C_x = A_2 a_{y1} - A_1 a_{y2} / a_{x2} a_{y1} - a_{x1} a_{y2} \quad c_y = A_1 a_{x1} - A_2 a_{x2} / a_{x2} a_{y1} - a_{x1} a_{y2}$$

$A_1 = 0.64$	$A_2 = 0.147$
$a_{x1} = 656$	$a_{x2} = 112$
$a_{y1} = 67$	$a_{y2} = 234$

$$\begin{aligned}
 C_x &= A_2 a_{y1} - A_1 a_{y2} / a_{x2} a_{y1} - a_{x1} a_{y2} \\
 &= 0.147 \times 67 - 0.664 \times 234 / 112 \times 67 - 656 \times 234 \\
 &= 9.84 - 155.37 / 7504 - 153504 \\
 &= -145.53 / 146000 \\
 &= 0.00099 \\
 &= 99 / 132 \times 472 = \mathbf{351.10} \\
 c_y &= A_1 a_{x1} - A_2 a_{x2} / a_{x2} a_{y1} - a_{x1} a_{y2} \\
 &= 0.664 \times 112 - 0.147 \times 656 / 146000 \\
 &= 74.36 - 96.4 / 146000 \\
 &= -22.04 / 146000 \\
 &= 0.00015 \\
 &= 15 / 132 \times 472 = \mathbf{51.63}
 \end{aligned}$$

The amount of Paracetamol and the Diclofenac was found to be **351.10mg** and **51.63mg**

Validation:

The method was validated for several parameters like linearity, accuracy, precision, Ruggedness, Robustness, Limit of detection (LOD), limit of quantification (LOQ) according to ICH guidelines.

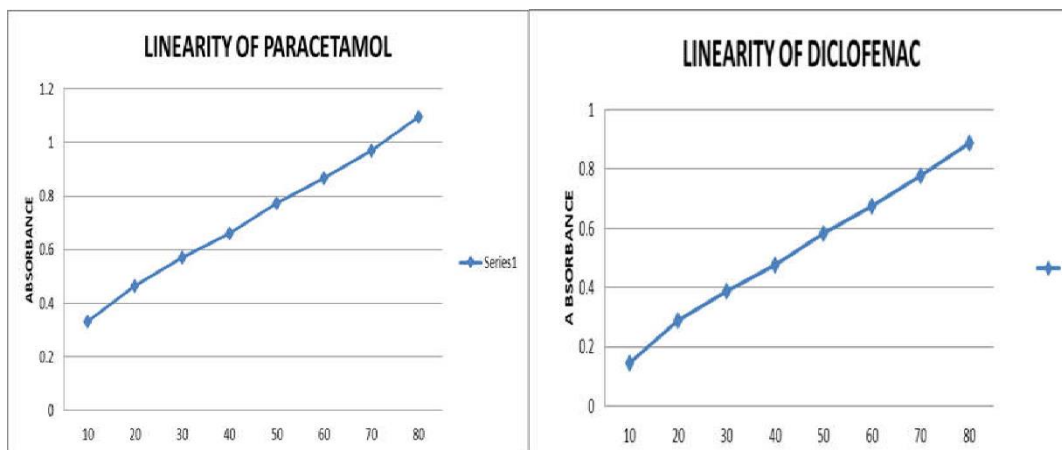


Fig.7: Calibration curve of Paracetamol and Diclofenac

Linearity:

Precision:

Precision results showing repeatability of Diclofenac:

Concentration($\mu\text{g/ml}$)	Absorbance	StatisticalAnalysis
10	0.147	
10	0.147	Mean=0.147
10	0.148	S.D=0.00075
10	0.147	%RSD=0.26%

Precision results showing repeatability of Paracetamol:

Concentration($\mu\text{g/ml}$)	Absorbance	StatisticalAnalysis
20	0.664	
20	0.665	Mean=0.664
20	0.664	S.D=0.00092
20	0.666	%RSD=0.72%

Accuracy:

Accuracy readings of Diclofenac Sodium Tablets:

Labelled claim (mg)	Level of Addition (%)	Amount of pure drug added (mg)	%Recovery	Statistical Analysis		
				MEAN	SD	%RSD
40	80	80	100.0	99.7	0.9316	0.91
40	80	80	99.43			
50	100	100	101.2			
50	100	100	99.60	100.06	0.8563	0.97
60	120	120	98.10			
60	120	120	100.0	99.17	0.9724	0.98

Accuracy readings of paracetamol:

Labelled claim (mg)	Level of Addition(%)	Amount of pure drug added(mg)	%Recovery	Statistical Analysis		
				MEAN	SD	%RSD
350	80	80	100.34	99.91	0.9016	0.90
350	80	80	99.8			
350	100	100	99.53	100.4	0.8	0.94
350	100	100	100.4			
350	120	120	98.8			
350	120	120	100.0	99.17	0.9724	0.98

LOQ and LOD:

LOQ and LOD was determined using the following equation $LOQ=10s/m$, $LOD=3.3s/m$ where s is the standard deviation of the response and m is the slope of the related calibration curve. The values of LOQ and LOD for paracetamol was found to be 9.26 and $2.40\mu\text{g/ml}$ and for diclofenac and 4.13 and $1.80\mu\text{g/ml}$ respectively.

RESULTS AND DISCUSSION:

The wave length corresponding to maximum absorbance in buffer solution was found at 242 and 276nm. Beer law was obeyed in the concentration range of 10-80µg/ml with correlation coefficient 0.9905. Accuracy of the proposed method was determined by the recovery studies, and good %recovery (98-102%) of the drugs obtained indicate that the method is accurate. The method was found to be precise as %RSD values for interday (0.43%) and intraday (0.34%) for diclofenac and for the paracetamol intraday (0.67%) interday(0.73%) was found to be less than 2. The method was also found to be and robust for diclofenac(0.30%) and for the paracetamol(0.36%) as the % RSD values were found to be less than 2. The limit of detection and limit of quantification of the proposed method for paracetamol 9.26 and 2.40 µg/ml and for the diclofenac 4.13 and 1.80 µg/ml indicating that the method developed is sensitive. The results of assay obtained were found to be in good agreement with the labelled claim, indicating the absence of interference of the excipients.

CONCLUSION:

The proposed UV spectrophotometric method is a simple, accurate, precise, rapid and economical for simultaneous estimation of Paracetamol and Diclofenac sodium in tablet dosage form. The proposed method uses inexpensive reagents, solvents and instruments that are available in laboratories. Hence, these methods can be conveniently adopted for routine analysis in quality control laboratories.

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