Available Online at

http://www.ijcpa.in

July - September 2016

DOI : http://dx.doi.org/10.21276/ijcpa

International Journal of CHEMICAL AND PHARMACEUTICAL ANALYSIS

eISSN: 2348-0726 ; pISSN : 2395-2466

Research Article | Volume-3 | Issue-4 | Article ID: 1036

METHOD DEVELOPMENT AND VALIDATION FOR THE SIMULTANEOUS ESTIMATION OF PARACETAMOL AND DICLOFENAC BY UV SPECTROSCOPY IN TABLET DOSAGE FORM

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Received: 16 May 2016 / Revised: 12 September 2016 / Accepted: 19 September 2016 / Available online : 30 September 2016

ABSTRACT

A simple, rapid, accurate, precise, and economic spectrophotometric method for simultaneous estimation of paracetamol and diclofenac in tablet dosage form have been developed and validated. Paracetamol and diclofenac show absorbance maximums at 242 and 273nm respectively by using 6.8 phosphate buffers, so absorbance was measured at the same wave lengths for the estimation of paracetamol and diclofenac. Absorbance is measured at 240.2 nm (Isoabsorptive point) and 258.4nm (λmax of diclofenac). Both drugs obey the Beer's Lambert's law in the concentration range of 10-30 µg/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, Methanol, UV Spectroscopy*

1. INTRODUCTION

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

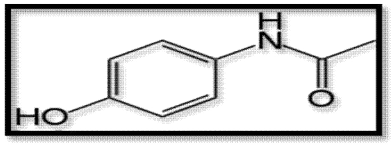

Fig.1: Structure of Paracetamol

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.

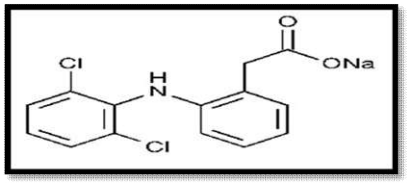

Fig.2: Structure of Diclofenac sodium

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.

2. MATERIALS AND METHODS

2.1 Instrumentation

1. Single pan balance (Calon).
2. Digital PH meter (ME-962P)
3. UV Double beam spectrophotometer 2202 (Systronics), Path length 1cm,
   UV Range:200-400 nm, Λmax:254 nm.

2.2 Reagents and Chemicals

Methanol, Sodium Hydroxide, Hydrogen Chloride,Distilled Water

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

2.3 Determination of maximum wavelength (λ_{max}) for paracetamol

2.3.1 Preparation of stock solution

Standard stock solution of paracetamol was prepared by dissolving accurately weighed 100mg of paracetamol in 6.8 buffer solution in a 100ml volumetric flask from this 1ml is taken and dissolved in 100ml buffer solution. The samples 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 242nm.

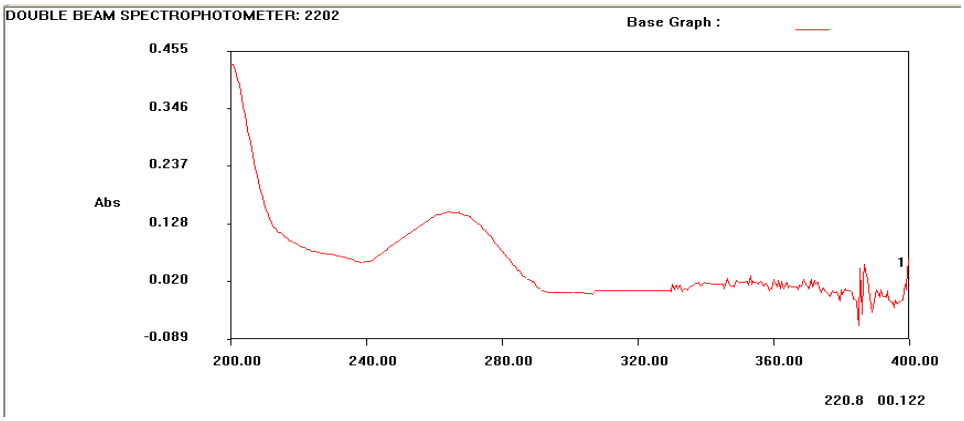

Fig. 3 : UV Spectrum of Paracetamol

2.4 Determination of maximum wavelength (λmax) for Diclofenac

2.4.1 Preparation of stock solution

Standard stock solution of diclofenac was prepared by dissolving accurately weighed 100mg of diclofenac in 6.8 buffer solution in a 100ml volumetric flask from this 1ml is taken and dissolved in 100ml buffer solution . The samples 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 273nm.

2.5 Isobestic point for the paracetamol and diclofenac

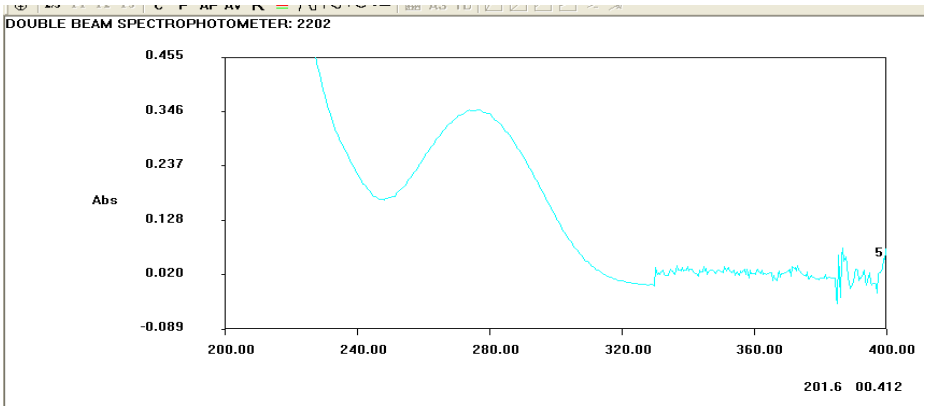

Fig. 4 : UV Spectrum of Diclofenac

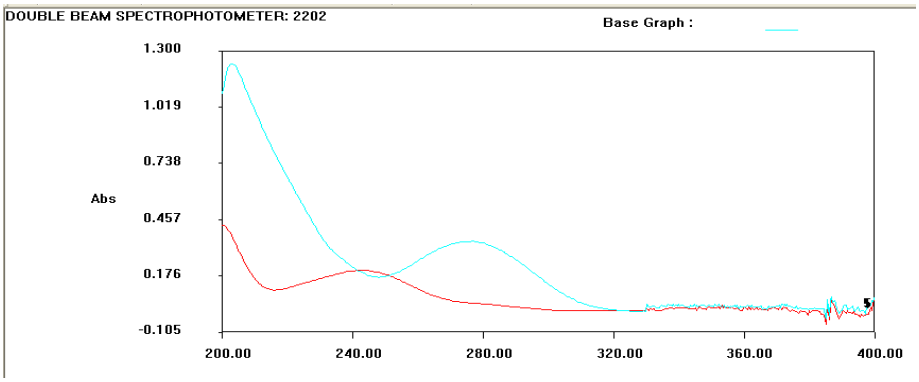

Fig. 5 : Overlaid UV Spectrum of Paracetamol and Diclofenac

2.6.Determination of maximum wavelength (λmax) for Paracetamol and Diclofenac:

2.6.1 Preparation of sample solution- Sample stock solution of paracetamol and diclofenac was prepared by dissolving accurately weighed 132mg of paracetamol and diclofenac in 6.8 buffer solution in a 100ml volumetric flask from this 1ml is taken and dissolved in 100ml buffer solution . The samples 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 242nm and 273nm.

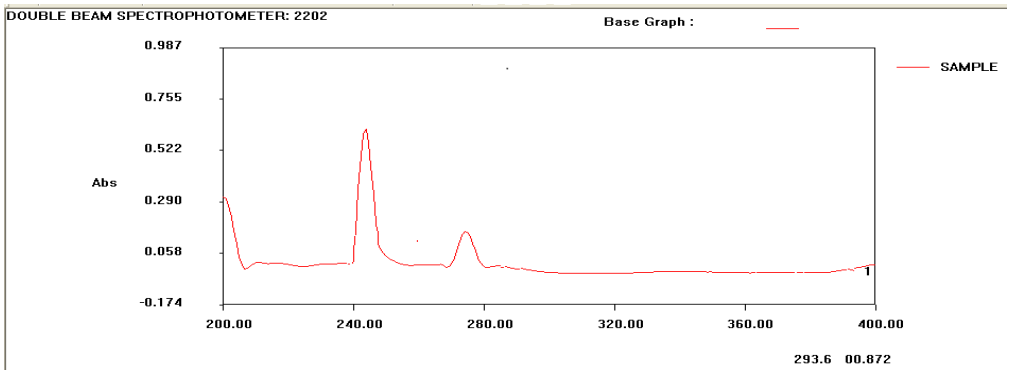

Fig. 6 : UV Spectrum of Paracetamol and Diclofenac solution

2.7 Absorbance of paracetamol and diclofenac and its λmax

WAVELENGTH	PARACETAMOL	DICLOFENAC	SAMPLE	ABSORBANCE OF PARACETAMOL	ABSORBANCE OF DICLOFENAC
242	0.656	0.67	0.664	656	67
273	0.112	0.234	0.147	112	234

2.8 Simultaneous equation method

$C_x = A_2ay_1 - A_1ay_2/ax_2ay_1-ax_1ay_2$ $c_y = A_1ax_1-A_2ax_2/ax_2ay_1-ax_1ay_2$

A_1=0.64	A_2=0.147
ax_1=656	ax_2=112
ay_1=67	ay_2=234

$C_x = A_2ay_1 - A_1ay_2/ax_2ay_1-ax_1ay_2$

= 0.147× 67- 0.664× 234 /112×67-656×234

= 9.84-155.37/7504-153504

= -145.53/146000

= 0.00099

= 99/132×472**= 351.10**

$c_y = A_1ax_1-A_2ax_2/ax_2ay_1-ax_1ay_2$

= 0.664×112-0.147×656/146000

= 74.36-96.4/146000

= -22.04/146000

= 0.00015

= 15/132×472 = **51.63**

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

2.9 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.

2.9.1 Linearity

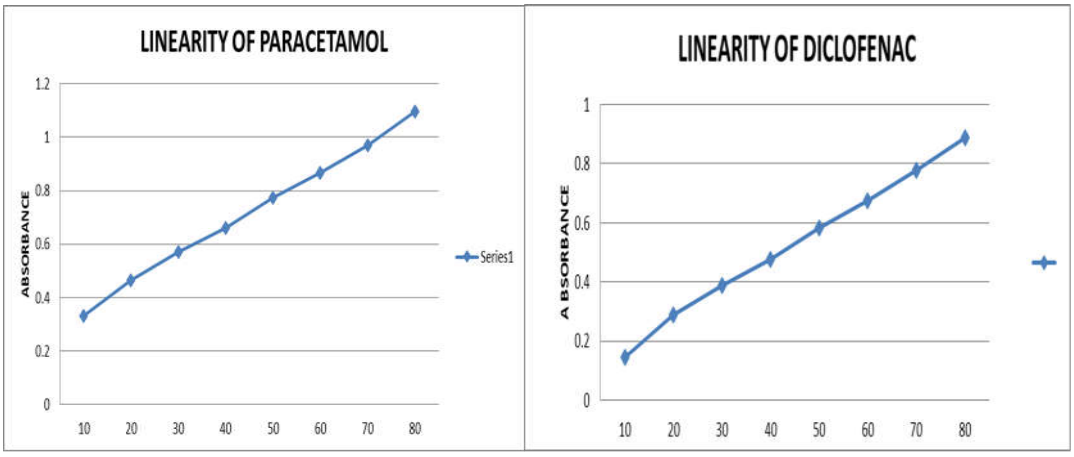

Fig. 7 : Calibration curve of Paracetamol and Diclofenac

2.9.2 Precision

a) Precision results showing repeatability of Diclofenac

Concentration (µg/ml)	Absorbance	Statistical Analysis
10	0.147	
10	0.147	Mean = 0.147
10	0.148	S.D = 0.00075
10	0.147	%RSD = 0.26%

b) Precision results showing repeatability of Paracetamol

Concentration (µg/ml)	Absorbance	Statistical Analysis
20	0.664	
20	0.665	Mean =0.664
20	0.664	S.D =0.00092
20	0.666	%RSD = 0.72%

2.9.3 Accuracy

a) 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

b) 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

2.9.4 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 2.40µg/ml and for diclofenac and 4.13 and 1.80µg/ml respectively.

3. RESULTS AND DISCUSSION

The wavelength corresponding to maximum absorbance in buffer solution was found at 242 and 273nm. Beers 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 4.13and 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.

4. 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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