Available Online through
www.ijpbs.com (or) www.ijpbsonline.com

IJPBS |Volume 2| Issue 4 |OCT-DEC |2012|37-48

Research Article
Pharmaceutical Sciences

SPECTROPHOTOMETRIC METHODS FOR SIMULTANEOUS ESTIMATION OF RABEPRAZOLE AND DICLOFENAC FROM COMBINED DOSAGE FORM

T Gopiraju, A Rajesh, M Gayatri Ramya, Y Surendra*

**Department of pharmaceutical chemistry, Telangana University, Dichpally, Nizamabad,*
Department of Pharmaceutics, Shadan college of pharmacy, peerancheru,Hyderabad,
Department of Pharmaceutics, Tallapadmavathi college of Pharmacy, orus , Kareemabad, Warangal

ABSTRACT

A novel, simple, safe, sensitive, and economical method of spectrophotometric estimation in UV region has been developed for Rabeprazole sodium and Diclofenac sodium in combined dosage form. The proposed methods are precise, accurate and do not suffer from any interference due to common excipients and/or degraded impurities. According to ICH norms the parameters linearity, precision, accuracy, limit of detection, and limit of quantification were studied, the results of analysis were validated statistically and by recovery studies. The proposed methods were simple, cost effective and were successfully applied to the determination of these drugs in quality control of combined pharmaceutical dosage.

INTRODUCTION

Rabeprazole and Diclofenac are the anti ulcerative and Non-steroidal anti-inflammatory drugs respectively. Rabeprazole is not official in any of the pharmacopoeias and diclofenac are official in IP, BP, EP and USP [1-5, 24.] Rabeprazole belongs to the class of antisecreatory compound that neither exihibit anticholinergic nor histamine H-2 receptor antagonistic properties, but suppress gastric acid secretion by inhibiting gastric H+ K+ATPase at the secretory surface of the of the gastric parietal cell.[6-11] Diclofenac inhibits Prostaglandin (PG) synthesis by inhibiting Cyclooxygenase enzyme1. HPLC methods are reported for the individual estimation of Rabeprazole and Diclofenac in the tablet dosage form.[12-14]

MATERIAL AND METHODS

Instrumentation

UV/visible double beam spectrophotometer (Shimadzu Model 1700) was employed with spectral bandwidth of 1nm and wavelength accuracy of ±0.3 nm (with automatic wavelength correction with a pair of 1 cm matched quartz cells).

REAGENTS AND CHEMICALS

Analytical pure standard samples of RS and DS were supplied as gift sample by Zydus cadila, India and Ranbaxy Laboratories Ltd., Ipca Labs, India respectively and used without further purification. The Pharmaceutical dosage form used in study was a R Clonac (Label claim: 20 mg of RS as enteric coated pellets and 100mg of DS I.P. as sustained release pellets) manufactured by Lupin,India.

Preparation of standard stock solution of Rabeprazole Sodium [15]

Accurately weighed Rabeprazole Sodium (10 mg) was transferred to 100 ml volumetric flask,

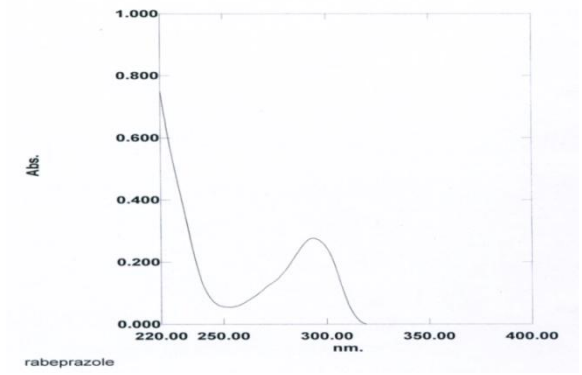
dissolved in methanol: 0.1N NaOH (50:50) and made-up the volume to 100 ml with same solvent system. The final solution contained 100 µg per ml of Rabeprazole Sodium solution.

Preparation of standard stock solution of Diclofenac Sodium [16]

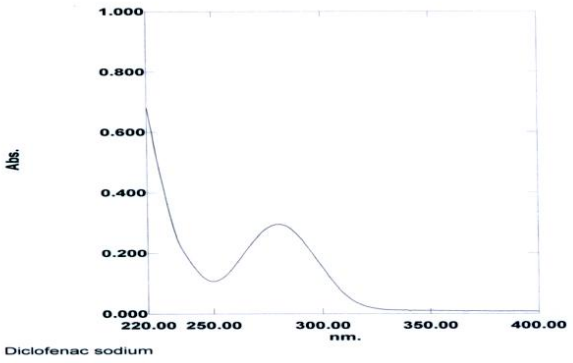
Accurately weighed Diclofenac Sodium (10 mg) was transferred to 100 ml volumetric flask, dissolved in methanol:0.1N NaOH (50:50) and made-up the volume to 100 ml with same solvent system. The final solution contained 100 µg per ml of Diclofenac Sodium solution.

Determination of wavelength of maximum absorbance for Rabeprazole Sodium [17]

Standard Rabeprazole Sodium solution (1ml) was transferred to separate 10 ml volumetric flask. The volume was adjusted to 10 ml with same solvent mixture. The absorbance of the final solution was scanned in the range 400 to 220 nm against solvent mixture as blank.



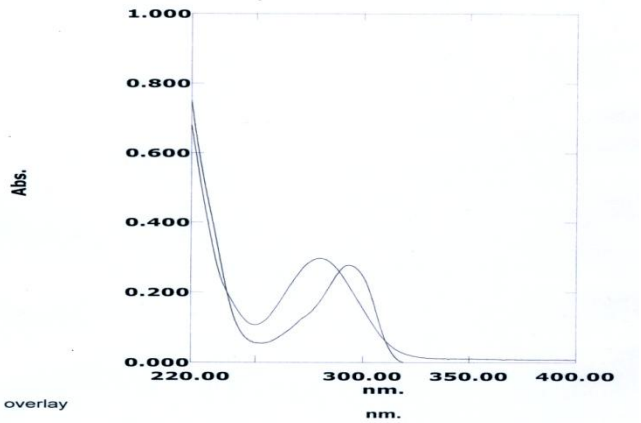
Spectrum of λ max. of Rabeprazole Sodium (293.8 nm)



Spectrum of λ max. of Diclofenac Sodium (279.8 nm)

Determination of wavelength of maximum absorbance for Diclofenac SodiumStandard Diclofenac Sodium solution (1 ml) was transferred to separate 10 ml volumetric flask. The volume was adjusted to 10 ml with same solvent mixture. The absorbance of the final solution was scanned in the range 400 to 220 nm against solvent mixture as blank.

The overlain spectra of Rabeprazole Sodium and Diclofenac Sodium



Overlain spectra of λ max. of Rabeprazole Sodium (293.8 nm) and Diclofenac Sodium (279.8 nm).

The above figure concludes that both the drugs absorbs at the λ max. of the other so, it may be possible to determine both the drugs by Simultaneous equation method/Vierodt's method.

Preparation of calibration curve for Rabeprazole Sodium and Diclofenac Sodium [18]

Standard solutions of Rabeprazole Sodium in the concentration range of 2 µg/ml to 80 µg/ml were obtained by transferring (0.2,1,2,3,4,5,6,7,8 ml) of Rabeprazole stock solution (100 ppm) to the series of 10 ml volumetric flasks and standard solutions of Diclofenac Sodium in the concentration range of 5 µg/ml to 70 µg/ml were obtained by transferring (0.5,1,2,3,4,5,6,7 ml) of Diclofenac Sodium stock solution (100 ppm) to the series of 10 ml volumetric flasks. The volumes in each volumetric flask were made up with the solvent system and mixed.

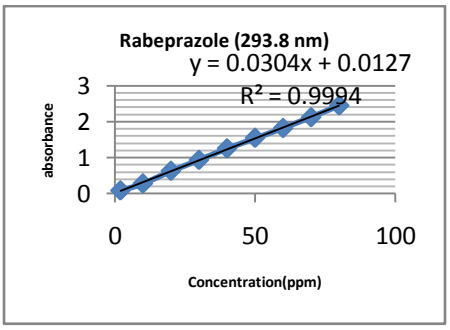
The absorbances of the solutions were measured at 279.8 nm and 293.8 nm against the solvent system as blank and calibration curves were plotted. The Lambert-Beer's Law is linear in concentration range of 2 to 80 µg/ml at 279.8 nm and 2 to 80 µg/ml at 293.8 nm for Rabeprazole Sodium. The Lambert-Beer's Law is linear in concentration range of 5 to 70 µg/ml at 279.8 nm and 5 to 70 µg/ml at 293.8 nm for Diclofenac Sodium.

Absorptivities of Rabeprazole Sodium

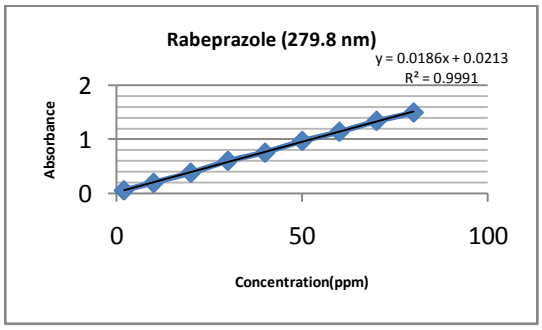
Conc. (µg/ml)	Absorbance		Absorptivity Coefficient	
	At 293.8 nm	At 279.8 nm	a_{x1} At 293.8 nm	a_{x2} At 279.8 nm
2	0.083	0.060	41.50	30
10	0.278	0.197	27.80	19.70
20	0.629	0.383	31.45	19.15
30	0.933	0.602	31.10	20.06
40	1.253	0.752	31.32	18.80
50	1.548	0.968	30.96	19.36
60	1.819	1.136	30.31	18.93
70	2.121	1.336	30.30	19.08
80	2.448	1.490	30.60	18.62
MEAN			31.70	20.41
S.D			3.83	3.62

Absorptivities of Diclofenac Sodium

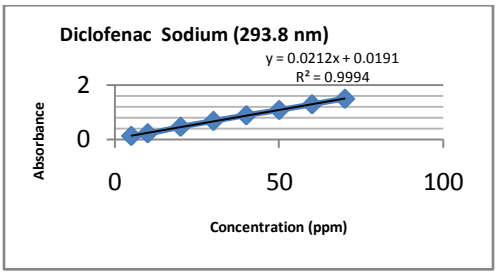
Conc. (µg/ml)	Absorbance		Absorptivity Coefficient	
	At 293.8 nm	At 279.8 nm	a_{y1} At 293.8 nm	a_{y2} At 279.8 nm
5	0.116	0.161	23.20	32.20
10	0.215	0.296	21.50	29.60
20	0.455	0.593	22.75	29.65
30	0.672	0.856	22.40	28.53
40	0.881	1.198	22.02	29.95
50	1.077	1.455	21.54	29.10
60	1.289	1.792	21.48	29.86
70	1.493	2.049	21.32	29.27
MEAN			22.02	29.77
S.D			0.69	1.08



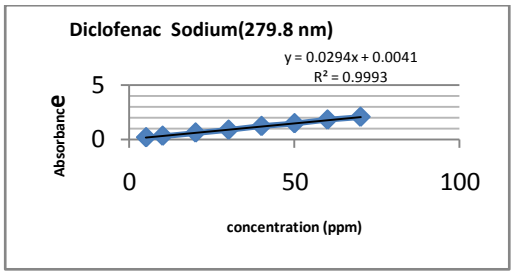
Calibration curve for Rabeprazole Sodium at 293.8 nm.



Calibration curve for Rabeprazole Sodium at 279.8 nm.



Calibration curve for Diclofenac Sodium at 293.8 nm.



Calibration curve for Diclofenac Sodium at 279.8 nm.

Determination of optical parameters

The Molecular absorptivity and Sandell's sensitivity were calculated as

Molecular absorptivity (Є) = AM/ct

A = Absorbance

M = Molecular weight

C = Concentration of sample

t = path length

Sandell's Sensitivity = M/Є

M = molecular weight

Є = Molecular absorptivity

Other optical parameters i.e. Beer's limit, slope, intercept and correlation coefficient were calculated from calibration curve.

Preparation of API mixtures of Rabeprazole Sodium and Diclofenac Sodium [19]

The API mixture of Rabeprazole Sodium and Diclofenac Sodium were prepared in ratio of 1:5. Accurately weighed 20 mg of Rabeprazole Sodium and 100 mg of Diclofenac Sodium were transferred to 100 ml volumetric flask, and volume was made up to mark with the solvent. Then 10 ml of the solution was diluted to 100 ml with the solvent system. The decision of this ratio of drugs in the API mixture was based upon the dosage strength of combination, which is available in the market.

Estimation of Rabeprazole Sodium and Diclofenac Sodium in synthetic mixture [20]

The API mixture (1, 2.5, 4, 5.5, 7 ml) were transferred to a series of five 10 ml volumetric flasks separately and volume was made up to the mark with solvent system . The absorbances of these solutions were measured at 293.8 nm and 279.8 nm which are shown in table 12.

At 293.8 nm and 279.8 nm two simultaneous equations were formed using absorptivity coefficient values.

At λ_1, $A_1 = a_{x1}bC_x + a_{y1}bC_y$ ----------(1)

At λ_2, $A_2 = a_{x2}bC_x + a_{y2}bC_y$ ----------(2)

For measurement in 1 cm cells, b = 1.

Rearranging equation (2),

$$C_Y = \frac{(A_2 - a_{x2} C_x)}{a_{y2}} \quad \text{---------- (3)}$$

Substituting the value for C_y in equation (1), we have:

$$C_X = \frac{(A_2\, a_{y1} - A_1\, a_{y2})}{(a_{x2}a_{y1} - a_{x1}\, a_{y2})} \quad \text{---------- (4)}$$

and,

$$C_Y = \frac{(A_1\, a_{x2} - A_2\, a_{x1})}{(a_{x2}\, a_{y1} - a_{x1}\, a_{y2})} \quad \text{---------- (5)}$$

Where C_X and C_Y are concentration of Rabeprazole Sodium and Diclofenac Sodium respectively in gm/liter in the sample solution. A_1 and A_2 are the absorbance's of the mixture at 293.8 nm and 279.8 nm respectively.

Two simultaneous equations were formed using the absorptivity coefficient values. 31.70 and 22.02 are absorptivities at 293.8 nm for Rabeprazole Sodium and Diclofenac Sodium respectively, while 20.41 and 29.77 are absorptivities at 279.8 nm for Rabeprazole Sodium and Diclofenac Sodium respectively.

$A_1 = 31.70\ C_x + 22.02\ C_y$ ..... (10)

$A_2 = 20.41\ C_x + 29.77\ C_y$ ..... (11)

Value of absorptivities

a_{x1}	a_{x2}	a_{y1}	a_{y2}
31.70	20.41	22.02	29.77

Putting the value of ax1, ax2, ay1, ay2 in equation (4) and (5), new equations are formed as follows-

$$C_X = \frac{A_2\ 22.02 - A_1\ 29.77}{-494.281} \quad \text{--- (12)}$$

$$C_Y = \frac{A_1\ 20.41 - A_2\ 31.70}{-494.281} \quad \text{--- (13)}$$

Absorbances for API mixture in 1: 5 (RAB: DCL) ratio

Mixture	Conc. (µg/ml)	WL. (nm)	Absorbance			Mean ± S.D.	Conc. (µg/ml)
			A	B	C		
1	2	293.8	0.287	0.287	0.289	0.287±0.0012	2.183
	10	279.8	0.338	0.338	0.342	0.339±0.0023	9.89
2	5	293.8	0.706	0.704	0.704	0.705±0.0011	4.951
	25	279.8	0.842	0.841	0.842	0.842±0.0006	24.889
3	8	293.8	1.138	1.139	1.135	1.137±0.0021	7.893
	40	279.8	1.358	1.36	1.362	1.360±0.0020	40.272
4	11	293.8	1.554	1.553	1.554	1.554±0.0006	10.867
	55	279.8	1.856	1.856	1.859	1.857±0.0017	54.928
5	14	293.8	1.987	1.987	1.988	1.987±0.0005	14.092
	70	279.8	2.37	2.372	2.369	2.370±0.0015	69.949

Validation of the developed method according to I.C.H guidelines [22]

Following parameters were taken into consideration for validation of proposed methods:

Specificity

Method: The synthetic mixture of Rabeprazole Sodium and Diclofenac Sodium was prepared in ratio of 1:5. Accurately weighed 20 mg of Rabeprazole Sodium and 100 mg of Diclofenac Sodium were transferred to 100 ml volumetric flask, and 70 ml of solvent system was added. Common excipients, such as 25.44 mg of starch, 22.26 mg of magnesium stearate and 270.30 mg of lactose (for 1000 µg/ml) which were used in tablet formulation, were added in this mixture and sonicated for 20 minutes. This solution was filtered through the Whatmann filter paper and

residues were washed with solvent system. The filtrate and washings were combined and volume was made-up to the 100 ml with solvent system.

Formulation of synthetic mixture is given as follows-

Averge weight of one tablet = 438 mg
Content of Diclofenac Sodium present = 100 mg
Content of Rabeprazole Sodium present = 20 mg
Weght of excipients=(438-120) = 318 mg
Weight of starch added = 25.44 mg
Weight of magnesium sterate added = 22.26 mg
Weight of lactose added =270.30 mg

Then 10 ml of the solution was diluted to 100 ml with the solvent system. From this stock solution, synthetic mixture (1, 2.5, 4, 5.5, 7 ml) were transferred to a series of five 10 ml volumetric flasks separately and volume was made upto the mark with solvent system. The absorbances of these solutions were measured at 293.8 nm and 279.8 nm which are shown in table 13. The decision of this ratio of drugs in the synthetic mixture was based upon the dosage strength of combination, which is available in the market.

Specificity study for the synthetic mixture in 1: 5 (RAB: DCL) ratio

Mix	Conc. (µg/ml)	λ_{max} (nm)	Before addition of excipients		After addition of excipients		% Inter-ference
			Abs.	Conc. (µg/ml)	Abs.	Conc. (µg/ml)	
1	2:10	293.8	0.287	2.183	0.291	2.202	0.870
		279.8	0.339	9.89	0.344	10.046	1.577
2	5:25	293.8	0.705	4.951	0.707	4.937	-0.283
		279.8	0.842	24.889	0.845	24.999	0.442
3	8:40	293.8	1.137	7.893	1.129	7.904	0.139
		279.8	1.36	40.272	1.349	40.03	-0.601
4	11:55	293.8	1.554	10.867	1.558	10.974	0.985
		279.8	1.857	54.928	1.86	54.955	0.049
5	14:70	293.8	1.987	14.092	1.982	13.836	-1.816
		279.8	2.37	69.949	2.369	70.091	0.203
Mean	**RAB**						-0.021
	DCL						0.334

Limit of detection and limit of quantification

The detection limit (LOD) and quantitation limit (LOQ) may be expressed as:

L.O.D. = 3.3(SD/S).
L.O.Q. = 10(SD/S)

Where, SD = Standard deviation of the response
S = Slope of the calibration curve

The slope S may be estimated from the calibration curve of the analyte.

The results are shown in Table.

Limit of Detection and Quantification

S. No.	(x) Slope RAB	(x) Slope DCL	(y) Intercept RAB	(y) Intercept DCL	L.O.D	L.O.Q
1	0.0304	0.0294	0.0127	0.0041	**RAB**	**RAB**
2	0.0303	0.0293	0.0134	0.0088	0.2420	0.7335
3	0.0303	0.0295	0.0146	0.0083		
4	0.0305	0.0292	0.0104	0.0086	**DCL**	**DCL**
5	0.0304	0.0293	0.0114	0.0065	0.2011	0.6096
6	0.0306	0.0292	0.0084	0.0077		
Mean	0.03042	0.02932				
S.D.			0.00223	0.00179		

Estimation of Rabeprazole Sodium and Diclofenac Sodium in tablet dosage form

Twenty tablets were taken and the I.P. method was followed to determine the average weight.

Method: Above weighed tablets were finally powdered and triturated well. A quantity of powder equivalent to 120 mg of drugs were transferred to 100 ml volumetric flask, and mixed with 70 ml of methanol:0.1N NaoH (50:50). and solution was sonicated for 10 minutes there after volume was made up to 100 ml with same solvent system. The solution was filtered through Whatmann filter paper. Then 10 ml of the above filtrated solution was diluted to 100 ml with the solvent system .From this stock solution (3.75 ml) was transferred to five different 10 ml volumetric flasks and volume was made up to 10 ml with same solvent system. The absorbance's of these solutions were measured at 293.8 nm and at 279.8 nm using methanol:0.1 NaoH (50:50) as blank.[23]

Percent tablet claim for Rabeprazole Sodium and Diclofenac Sodium tablets was determined by using equation 4 and 5.

Average Weight of 20 Tablet

TABLET	AVERAGE WEIGHT (mg)
R Clonac	438

The developed method was evaluated in the assay of commercially available tablets containing 20 mg of Rabeprazole Sodium and 100 mg of Diclofenac Sodium.

Statistical Analysis for R Clonac Tablet

(For RAB 7.5 µg/ml; DCL 37.5 µg/ml respectively)

S. No.	Absorbance Data		Conc. Found in µg/ml		Labelled amount in tablet (mg/tab)	Amount found in (mg/tablet)	
	293.8 nm	279.8 nm	RAB	DCL	RAB : DCL	RAB	DCL
1	1.063	1.268	7.534	37.428	20 : 100	20.091	99.808
2	1.061	1.267	7.459	37.446		19.890	99.856
3	1.059	1.265	7.427	37.4		19.805	99.733
4	1.062	1.268	7.474	37.469		19.931	99.917
5	1.06	1.266	7.443	37.423		19.848	99.794
Mean			**7.467**	**37.433**		**19.913**	**99.822**

RESULT & DISCUSSION

For Rabeprazole Sodium the Beer- Lambert's law is obeyed in concentration range of 2 to 80 µg/ml both at 293.8 nm and at 279.8 nm . In the linearity study at respective wavelengths, the linear regression equation for Rabeprazole Sodium, calibration curve at 279.8 nm was calculated by y = 0.0186x + 0.0213,(R^2 = 0.9991) and calibration curve at 293.8 nm was calculated by y = 0.0304x + 0.0127,(R^2 = 0.9994), where y is absorbance and x is the value of various concentrations of standard solutions

For Diclofenac Sodium the Beer- Lambert's law is obeyed in concentration range of 5 to 70 µg/ml both at 293.8 nm and 279.8 nm .Moreover, in the linearity study at consecutive wavelengths, the linear regression equation for Diclofenac Sodium, calibration curve at 279.8 nm was calculated by y = 0.0294x + 0.0041 (R^2 = 0.9993) and calibration curve at 293.8 nm was calculated by y = 0.0212x + 0.0191 (R^2 = 0.9994). The results obtained for the specificity study from five samples studies (n = 3) after addition of excipients had a very negligible change in concentration as compare to concentration before addition of excipients. It can be concluded from the results that developed method is specific as percent interference was found to be -0.021 and 0.334 for Rabeprazole Sodium and Diclofenac Sodium respectively, which is less than 0.5 %.

Linearity range was found to be 2-80 µg/ml for Rabeprazole Sodium at 293.8 nm and 279.8 nm.The correlation coefficient was found to be 0.9994 & 0.9991 respectively, which adhere good linearity between above range. The slope was found to be 0.0304 & 0.0186 and intercept was found to be 0.0127 & 0.0213 which was close to zero intercept. For Diclofenac Sodium at 293.8 nm and 279.8 nm linearity range was found to be 5-70 µg/ml .The correlation coefficients was found to be 0.9994 & 0.9993 respectively, which adhere good linearity between above range. The slope was found to be 0.0212 & 0.0294 and intercept was found to be 0.0191 & 0.0041 which was close to zero intercept. In this case working range was found to be 0.7335 to 80 µg/ml & 0.6096 to 70 for Rabeprazole Sodium and Diclofenac Sodium respectively. Linearity range equal to 2-80 µg/ml & 5-70 µg/ml for Rabeprazole Sodium and Diclofenac Sodium. Target range: which is 80%,

100% and 120% of the target concentration. In this case these are equal to 30 µg/ml, 37.5 µg/ml and 45 µg/ml. Target concentration: It is defined as the concentration, which is equal to the midpoint of linearity range. It is equal [(70 +5)/2] =37.5 µg/ml.

The results obtained for the accuracy study (recovery method) from three sample studies (n = 3) for each level indicated that the mean of the % recovery was 99.383 % and 99.782 % and R.S.D was 0.757% and 0.216 % for Rabeprazole Sodium and Diclofenac Sodium respectively in synthetic mixture (RAB 2 µg/ml: DCL 10 µg/ml). Here the mean % recovery is in between 98-102 % thus showing that the analytical technique has a good recovery study.

Repeatability study showed a R.S.D of 0.437 % for Rabeprazole Sodium and 0.096 % for Diclofenac Sodium. Thus it is concluded that the analytical technique has a good repeatability precision as R.S.D for both drugs were less than 2 %. The LOD was found to be 0.2420 µg/ml and 0.2011 µg/ml and LOQ was found to be 0.7335 µg/ml and 0.6096 µg/ml for Rabeprazole Sodium and Diclofenac Sodium respectively which represents that sensitivity of the method is high. The amount of drug in tablet was found to be 19.913 mg/tab for Rabeprazole Sodium and 99.822 mg/tab for Diclofenac Sodium by Vierodt's method.

Optical and regression parameters of UV spectrophotometric method:

Parameters	Rabeprazole Sodium		Diclofenac Sodium	
	293.8 nm	279.8 nm	293.8 nm	279.8 nm
Beers's law limit (µg/ml)	2-80	2-80	5-70	5-70
Molar absorptivity (l mole^{-1}cm^{-1})	1.21x10^4	7.78x10^3	7.01x10^3	9.47x10^3
Sandell's sensitivity (mg/cm^2/.001absorb-ance unit)	0.0315	0.0490	0.0453	0.0335
Regression equation (y= a + bc) slope (b) intercept (a)	0.0304 0.0127	0.0186 0.0213	0.0212 0.0191	0.0294 0.0041
Correlation coefficient (r^2)	0.9994	0.9991	0.9994	0.9993

Summary of validation parameters by UV-Spectroscopy method

Validation parameters		RAB	DCL
Specificity		% interference <0.5 %	
Range (µg/ml)	Linear range	2-80	5-70
	Working range	0.734-80	0.609-70
	Target range	6,7.5,9	30,37.5,45
	Target concentration	7.5	37.5
Accuracy (% RSD)		0.757	0.216
Precision (% RSD)	Repeatability	0.437	0.096
	Intra day	0.743	0.246
	Inter day	1.373	0.497
LOD (µg/ml)		0.242	0.201
LOQ (µg/ml)		0.734	0.609

CONCLUSION

In the present work, U.V. spectrophotometric method for simultaneous estimation of Rabeprazole Sodium and Diclofenac Sodium in tablet has been developed. The proposed methods are precise, accurate and do not suffer from any interference due to common excipients and/or degraded impurities

The validation parameters according to I.C.H Q2B guidelines were studied. The accuracy of the methods was proved by performing recovery studies in available formulations. Values greater than 98% indicate that the proposed method is accurate for the analysis of drug.

REFERNCES

1. Michael E. S., Ira S. K., ''Analytical Method Development and Validation", Marcel Dekker, Inc., New York, 1997; 25-29.
2. Connors K.A, "A Text Book of Pharmaceutical Analysis", Wiley-Inter science, Singapore, 1999; 175.
3. http://www.pharmainfo.net/review/Introduction-analytical-method-development – pharmaceutical-formulations #content
4. Willard-H.H., Lynne L.M. Jr., John A., Dean F.A.," Instrumental Methods of Analysis", 7th Edn., CBS Publishers and Distributors, New Delhi ;1-12, 580-610, 614-652.
5. Davidson A.G, "Basis of Spectrophotometry", 4th Ed., Part-2, CBS Publishers, New Delhi, 2002; 264-74.
6. Fronk A.S.,"Handbook of Instrumental Techniques for Analytical Chemistry", 1st Edn., Pearson Education, 2004 ; 7.
7. Skoog D.A., Holler F.J., Nieman D.A.," Principle of Instrumental Analysis", 6th ed Reprint, Thomson Brooks/Cole publication, 2004 ; 300-351.(UV)
8. Sharma Y.R., "Elementary Organic Spectroscopy, Principle & Chemical Applications", S. Chand & Company Ltd., New Delhi, 2005; 8.
9. Kalsi P.S., "Spectroscopy of Organic Compounds", 5th ed, New Age International Publishers New Delhi, 2002; 7.
10. Braun R.D.,"Introduction to Instrument Analysis", Pharma Book Syndicate, Hyderabad, 2005; 261.
11. Beckett,A.H., Stenlake J.B., "Practical Pharmaceutical Chemistry", (1997), 4th edition, Part 2, CBS Publishers and Distributors ; 275-337.
12. Jadhav S. M. and Arbad B. R.; "Spectrophotometric methods for simultaneous estimation of tinidazole and nimesulide from tablet formulation" , The Indian Pharmacist, 2004,III (22) ; 63-65.
13. Dyer J.R., "Application of Absorption Spectroscopy of Organic Compounds", Prentice Hall of India Pvt. Ltd, New Delhi 2005.

14. Snyder L.R., Kirkland J.J. and Glajch L.J., "Practical HPLC Method Development", 2nd Edn., John Wiley and Sons, Inc., 1997; p.p. 2-18.
15. Sethi P.D., "High performance liquid chromatography: Quantitative analysis of pharmaceutical formulation", 2001; 1st Edn.; 5 – 11, 141.
16. Jens T. Carstensen, Rhodes C. T., "Drug stability principle and practices", 3rd Edn., Marcel Dekker Inc.; 331,338-339.
17. Nash R.A., Watcher A.H., "Pharmaceutical Process Validation", Marcel Dekker Inc.; New York, (2003); 507-522.
18. Validation of Analytical Procedure: Text and Methodology, ICH Harmonized Tripartite Guideline, Q2 (R1), 2005; 1-13.
19. http://www.mims.com/index.aspx?menuid=pgctrl&subid=brand&gen name=diclofenac sodium
20. http://en.wikipedia.org/wiki/diclofenac sodium
21. British Pharmacopoeia, Vol-I, The Department Of Health, The Stationery Office on behalf of the Medicines and Healthcare products Regulatory Agency (MHRA), London.
22. http://en.wikipedia.org/wiki/rabeprazole
23. http://chemicalland21.com/lifescience/uh/rabeprazole.htm.
24. Indian Pharmacopeia, 2007, Vol I, Govt. of India, Ministry of Health and Family Welfare, Ghaziabad.

***Corresponding Author:**
T.Gopiraju*
Department of pharmaceutical chemistry,
Telangana University,
Dichpally, Nizamabad