CODEN (USA): IAJPBB ISSN: 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

http://doi.org/10.5281/zenodo.268626

Available online at: http://www.iajps.com *Research Article*

SIMULTANEOUS ESTIMATION OF RABEPRAZOLE SODIUM AND ACECLOFENAC COMBINED CAPSULE DOSAGE FORM AS PER ICH GUIDELINE BY UV SPECTROSCOPIC METHODS

Ashok Patel, Arunoday Kumar Prajapati, Badaruddin, Vaishali Rathi, Kuldeep Patel*, Jagdish Chand Rathi*

NRI Institute of Pharmaceutical Sciences, 3, Sajjan singh Nagar, Raisen Bhopal,Madhya Pradesh - 462021 India.

Received: 12 October 2016 **Accepted:** 28 December 2016 **Published:** 31 January 2017

Abstract:

The present work aimed to develop and validate spectrophotometric methods for simultaneous estimation of rabeprazole sodium and aceclofenac in a pure and capsule dosage form. A simple, sensitive, spectrophotometric method in UV region has been developed for the simultaneous estimation of Rabeprazole sodium and Aceclofenac in bulk and semi dosage form (Capsule). Standard solution of Rabeprazole sodium shows maximum absorbance at 283 nm and Aceclofenac shows maximum absorbance at 276 nm. Beer's Lamberts law is obeyed in concentration range 10-60 µg/ml for Rabeprazole with regression, slope and intercept of 0.991, 0.0918 and 0 respectively while for, Beer's Aceclofenac Lambert law is obeyed in concentration range 10-60 µg/ml with regression, slope and intercept having 0.9984, 0.2069 and 0.0253 respectively. Method was validated for linearity, range, accuracy, precision, recovery studies and interference study of mixture. All these parameters showed the adaptability of the method for the quality control analysis of the drug in bulk and in combination formulations.

Keywords: *Rabeprazole sodium, Aceclofenac, Simultaneous equations, absorbance interference study.*

Corresponding Author:

Jagdish Chand Rathi, & Kuldeep Patel

Professor, Associate professor

NRI Institute of Pharmaceutical Sciences,

3, Sajjan singh Nagar, Raisen Bhopal,Madhya Pradesh - 462021 India.

E-mail: roshanrathi09@gmail.com Contact No.: +91-999377883.

QR code

Please cite this article in press as Jagdish Chand Rathi et al, ***Simultaneous Estimation of Rabeprazole Sodium and Aceclofenac Combined Capsule Dosage Form as Per ICH Guideline by UV Spectroscopic Methods****, Indo Am. J. P. Sci, 2017; 4(01).*

INTRODUCTION:

Rabeprazole sodium, chemically known as 2-[4-(3-methoxypropoxy)-3- methyl-2-pyridil]-methyl]sulfinyl]-1H-benzimidazole, is an anti-ulcerative drug. Rabeprazole sodium belongs to the class of antisecretory compounds that neither exhibit 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 gastric parietal cell. Second drug Aceclofenac, chemically known as [({2-[(2,6-dichlorophenyl) amino]phenyl} acetyl) oxy]acetic acid, is a non-steroidal anti-inflammatory drug(NSAID). It inhibits prostaglandin (PG) synthesis by inhibiting cyclooxygenase enzyme. Aceclofenac is official drugs in IP, BP, and USP whereas rabeprazole sodium is not. Literature survey reveals that UV spectrophotometric methods are reported for determination of aceclofenac Bombale et al. [1] and rabeprazole sodium individually in different pharmaceutical dosage forms. There are also various UV spectrophotometric methods available for estimation of aceclofenac or rabeprazole in combination with other drugs [2], but the UV spectrophotometric method for simultaneous estimation of rabeprazole sodium and aceclofenac is not yet reported. In this work, we propose two simple and validated UV spectrophotometric methods for simultaneous estimation of rabeprazole sodium and aceclofenac in pure and capsule dosage forms. The aim of the present investigation is to develop a simple, sensitive and reproducible UV Spectrophotometric method for analysis of Rabeprazole sodium and aceclofenac in a combined Capsule dosage form and hence an economical method was developed and validated according to the ICH guidelines (***ICH, Q2A, 1996***).

MATERIALS AND METHODS:

Instruments

A double beam UV-visible spectrophotometer, model- Shimadzu-1700, with a 1 nm resolution for spectral bandwidth in the scan mode (which can be one order of magnitude lower at a fixed wavelength setting). Such wavelength accuracy results in higher resolution and clearer readout of absorbance spectra with respect to other instruments in the same category. The wide wavelength range (190 to 1100 nm) and photometric range (Abs –0.5 to +3.0) make this spectrophotometer good for many different kinds of assays requiring UV/VIS excitation. The UV-1700 spectrophotometer reliability stems also from a nice photometric accuracy and repeatability (± 0.002 and ± 0.001, respectively, at 0.5 ABS as declared by Shimadzu). spectral band width of 1.5 nm and automatic wavelength corrections with a pair of 10 mm quartz cell was used for experimental work.

Reagents and chemicals

All reagents and chemicals used were of AR grade. The reference standard rabeprazole sodium and aceclofenac were obtained from Medico Remedies Pvt. Ltd,. Mumbai, as a gift sample. The commercially available capsule with brand name Nismol Plus (Neiss Lab) containing rabeprazole-20 mg and aceclofenac-200 mg was purchased from a local market.

Procedure

Preparation of standard stock solution and calibration curve

The standard stock solutions of Aceclofenac [Figure 1] and Rabeprazole sodium [Figure 2] were prepared by dissolving 10 mg. of each drug in methanol, and the final volume was adjusted with the same solvent in 10 ml of a volumetric flask to get a solution containing 1000 µg/ml of each drug. Working standard solutions of 10 µg/ml were scanned in the entire UV range of 400–200 nm to determine the λmax. The λmax of rabeprazole sodium and aceclofenac is 283 nm and 276 nm, respectively, and from overlain spectra [Figure 3] it is evident that the isosbestic point is at 256 nm. Six working standard solutions with a concentration of 10, 20, 30, 40, 50, and 60 µg/ml were prepared in methanol from stock solution. The absorbances of resulting solutions were measured at their respective λmax and the isosbestic point and plotted a calibration curve to get the linearity and regression equation [Figure 4 and 5].

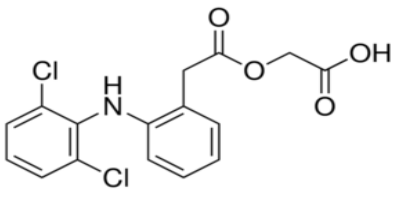

Fig. 1: Structure of Aceclofenac

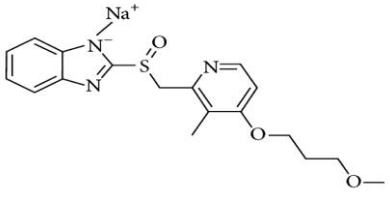

Fig. 2 Structure of Rabeprazole sodium

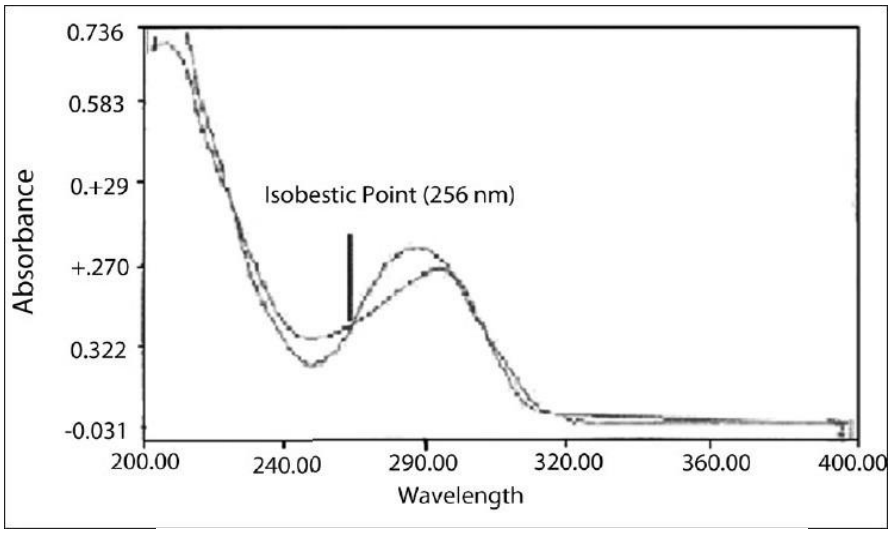

Fig.3: Overlain spectra of Aceclofenac and Rabeprazole sodium

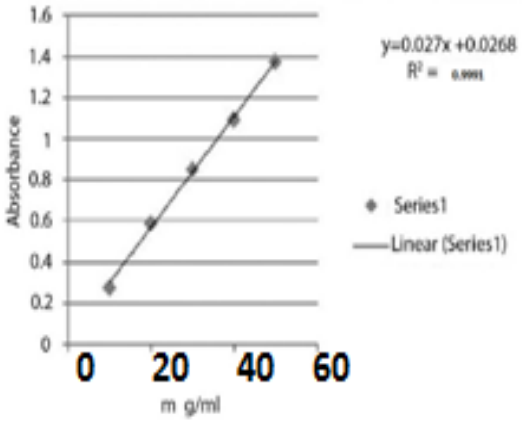

Fig. 4: Calibration curve of Rabeprazole

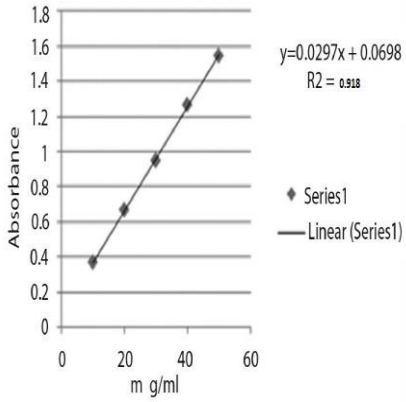

Fig. 5: Calibration curve of Aceclofenac

Method I: Simultaneous equations

The simultaneous equation method of analysis is based on the absorption of the drugs rabeprazole sodium and aceclofenac at their wavelength maxims. Two wavelengths selected for the development of the simultaneous equations are 283 nm and 276 nm. The absorptivity values are determined for rabeprazole sodium are 0.02803 (ax1), 0.02631 (ax2) and for aceclofenac 0.03022 (ay1), 0.03289 (ay2) at 283 nm and 276 nm, respectively. These values are average of six estimations. The absorbances and absorptivity at these wavelengths were substituted in equations (1) and (2) to obtain the concentration of drugs.

$Cx = A_2\ (0.03022) - A_1\ (0.03289)/0.00013$ ……..(1)

$Cy = A_1\ (0.02631) - A_2\ (0.02803)/0.00013$ ……..(2)

where A1 and A2 are the absorbance of sample solutions at 283 nm and 276 nm, respectively. Cx and Cy are concentrations of rabeprazole sodium and aceclofenac in µg/ml in sample solution. By substituting the values of A1 and A2,, the Cx and Cy can be calculated by solving equations (1) and (2).

Method II: Absorption ratio method

The absorbance ratio method of analysis is based on the absorbance at two selected wavelengths, one is an isosbestic point and the other being the wavelength of maximum absorption of one of the two components. From overlain spectra , wavelength 256 nm (isosbestic point) and 276 nm (λmax of aceclofenac) are selected for the formation of Q absorbance equation (equations 3 and 4). The absorptivity values determined for rabeprazole sodium are 0.01711 (ax1), 0.02632 (ax2) and for aceclofenac are 0.01876 (ay1), 0.03289 (ay2) at 283 nm and 256 nm, respectively. These values are average of six estimations. The absorbances and absorptivity at these wavelengths were substituted in equations (3) and (4) to obtain the concentration of drugs.

$Cx = (Q_m\ 1.7531)/(-0.215286) \times A_1 / 0.01711$ ……..(3)

$Cy = (Q_m\ 1.5378)/(0.215286) \times A_1 / 0.01876$ ……(4)

Q_M, Q_X, and Q_Y were obtained as below:

$Q_m = A_2/A_1$; $Q_x = ax_2/ax_1$; $Q_y = ay_2/ay_1 = 1.7531$

Where Cx and Cy are concentrations of rabeprazole sodium and aceclofenac, respectively, in mg/ml. A1 and A2 were the absorbance of the sample at 283 nm and 256 nm, respectively.

Validation of the developed methods

The following parameters are considered as ICH guidelines for the validation of the method.[11]

Linearity

For each drug, appropriate dilutions of standard stock solutions were assayed as per the developed methods. The Beer–Lambert's concentration range was found to be 10–60 µg/ml. The linearity data for both methods are presented in Table 1

Table 1: characteristics

Parameters	Method I		Method II	
	Rabeprazole	Aceclofenac	Rabeprazole	Aceclofenac
Wavelength λ_{max} (nm)	283	276	Isosbestic point at 256	
Beer's law limit (µg/ml)	10–60	10–60	10–60	10–60
Correlation coefficient R^2	0.9981	0.9997	0.997	0.998
Slope	0.027	0.0297	0.016	0.016
Intercept	0.0268	0.0698	0.013	0.034
Intra-day (%RSD)	0.215	0.431	1.21	0.83
Inter-day (%RSD)	0.612	0.764	0.725	1.16
LOD (µg/ml)	0.194	0.352	0.742	0.486
LOQ (µg/ml)	0.832	2.386	1.48	3.27

Precision

Intermediate precision (inter-day and intra-day precision)

The inter-day and intra-day precision was determined by the assay of the sample solution on the same day and on different days at different time intervals, respectively. The results of the same are presented in Table 1.

Limit of detection and limit of quantitation

The limit of detection (LOD) and limit of quantitation (LOQ) of rabeprazole sodium and aceclofenac by proposed methods were determined using calibration standards. LOD and LOQ were calculated as 3.3*s/S* and 10*s/S*, respectively,

where *S* is the slope of the calibration curve and *s* is the standard deviation of response. The results of the same are shown in Table 1

Accuracy

To check the accuracy of the proposed methods, recovery studies were carried out at 80%, 100%, and 120% of the test concentration as per ICH guidelines. The recovery study was performed three times at each level. The results of the recovery studies are quoted in Table 2

Table 2: Results of the recovery study

Drug	Level of recovery (%)	Method I					Method II				
		Amt. added (µg/ml)	Amt. estimated (µg/ml)	Recovery (%)	SD*	% R.S.D.*	Amt. added (µg/ml)	Amt. estimated (µg/ml)	Recovery (%)	SD*	% RSD*
RAB	80	1.6	3.59	99.44	0.844	0.848	1.6	1.59	99.99	0.13	0.1330
	100	2.0	4.05	101.2	0.944	0.933	2.0	2.004	100.2	1.091	1.088
	120	2.4	4.38	100.7	0.578	0.5739	2.4	2.403	100.14	0.14	0.1398
ACE	80	16	35.84	99.95	0.622	0.624	16	35.95	99.36	0.538	0.5414
	100	20	40.34	100.8	0.576	0.571	20	40.08	100.2	0.703	0.698
	120	24	43.52	98.92	1.283	1.297	24	44.02	100.06	0.14	0.1399

*Mean + SD of three observations

Table 3: Results of analysis of capsule

Method	Label claim (mg/Cap) (n = 6)	Amount found (mg)	% of drug content	SD	% RSD	SE
I	Rabeprazole (20 mg)	20.044	100.22	0.3518	0.35101	0.143
	Aceclofenac (200 mg)	199.92	99.96	0.05508	0.05509	0.032
II	Rabeprazole (20 mg)	19.98	99.99	0.130	0.130	0.028
	Aceclofenac (200 mg)	200.12	100.05	0.1242	0.1241	0.132

RESULTS AND DISCUSSION:

The linearity range for rabeprazole sodium and aceclofenac is 10–60 µg/ml and 10–60 µg/ml at respective selected wavelengths. The coefficient of correlation for rabeprazole at 283 nm and for aceclofenac at 276 nm is 0.9981 and 0.9997, respectively. Both drugs showed good regression values at their respective wavelengths, and the results of a recovery study revealed that any small change in the drug concentration in the solution could be accurately determined by the proposed methods. Percentage estimation of rabeprazole sodium and aceclofenac from the capsule dosage form by method 1 is 100.22 and 99.96 and by method 2 is 99.99 and 100.05, respectively, with standard deviation less than 2 [Table 3].

The validity and reliability of proposed methods were assessed by recovery studies. Sample recovery for both the methods is in good agreement with their respective label claims, which suggest noninterference of formulation additives in estimation [Table 2].

Precision was determined by studying the repeatability and intermediate precision. Repeatability indicates the precision under the same operating conditions over a short interval of time and inter-assay precision. The % RSD was calculated for rabeprazole sodium and aceclofenac. The results are mentioned in Table 1. An intermediate precision study expresses within a laboratory variation in different days. In intra- and inter-day precision studies for both the methods % RSD are not more than 2.0% indicates good repeatability and intermediate precision [Table 1].

The LOD and LOQ values for rabeprazole sodium and aceclofenac are 0.194, 0.352 µg/ml, and 0.832, 2.386 µg/ml by method 1 while the same by method 2 are 0.742, 0.486 µg/ml and 1.48, 3.27 µg/ml, respectively. Low values of LOD and LOQ indicates good sensitivity of proposed methods shown in Table 1

CONCLUSION:

The proposed methods are simple, rapid and validated in terms of linearity, accuracy, precision, specificity and reproducibility, and can be used successfully for routine simultaneous estimation of rabeprazole sodium and aceclofenac in pure and capsule dosage forms. Two new, simple, sensitive and economical UV spectrophotometric methods were developed for the simultaneous analysis of Rabeprazole sodium and Aceclofenac in bulk and in pharmaceutical formulations.

REFERENCES:

1. Rohit S, Chandrakant M, Shital KP, Dhanya K, Nilofar N. Validated spectroscopic method for estimation of aceclofenac from tablet. Res J Pharm Tech. 2008;1:430–2.
2. Maheshwari RK, Chaturvedi SC, Jain NK. Analysis of aceclofenac in tablets using hydrotropic solublisation technique. Indian Drugs. 2006;43:516–8.
3. Mallikarjuna GM, Somashekar S, Putta RK, Shanta SM. Physico-chemical characterization, UV spectrophotometric analytical method development and validation studies of rabeprazole sodium. J Chem Pharm Res. 2010;2:187–92.
4. Nafisur RZ, Syed NH. Quantitative analysis of rabeprazole sodium in commercial dosage forms by spectrophotometry. Chem Pharm Bull. 2008;56:995–1001.
5. Beckett, A.H., Stenlake, J.B (2005) Practical pharmaceutical chemistry, (4th ed., part II, pp.286) CBS publishers, New Delhi.
6.Bhatia, M.S., Kaskhedikar, S.G., Chaturvedi, S.C (1999) High performance liquid chromatographic estimation of Ciprofloxacin hydrochloride and Tinidazole from tablets.Indian Journal of Pharmaceutical Sciences,61(5), 311-312.
7. Bombale, M.V., Kadam, S.S., Dhaneshwar, S.R (1997) Simultaneous spectrophotometric estimation of Ciprofloxacin and Tinidazole from a combined dosage form. Indian Journal of Pharmaceutical Sciences, 59(5), 265-8.
8. Sharma, R., Pathodiya, G., Mishra, P.G., Sainy, J. A novel spectrophotometric method for quantitative determination of Ciprofloxacin hydrochloride and Tinidazole in tablets using hydrotropic solubilizing agent. Journal of Pharmacy Research, 2011;4(3): 859-861.
9. ICH, Q2A Text on validation of analytical procedures: Methodology International Conference on Harmonization of technical requirements for registration of pharmaceutical for human use. Geneva, Switzerland: 1996.
10. Sawant RL, Hadawale SD, Dhikale GK, Bansode CA, Tajane PS. Spectrophotometric methods for simultaneous estimation of rabeprazole sodium and aceclofenac from the combined capsule dosage form. Pharmaceutical Methods. 2011;2(3):193-197. doi:10.4103/2229-4708.90362.
11. ICH topic Q-2B Validation of analytical procedure: Methodology CPMP/ICH/281/95) the European agency for the evaluation of medicinal product, Human medicines evaluation unit, 1-9.
12. Synthesis of Some Coumarinyl Chalcones and their Antiproliferative Activity against Breast Cancer Cell Lines**.** Kuldeep Patel, Chandrabose Karthikeyan,

Viswas Raja Solomon, N.S. Hari Narayana Moorthy, Hoyun Lee, Kapendra Sahu, Girdhar Singh Deora and Piyush Trivedi. *Letters in Drug Design & Discovery, 2011, Vol. 8, No* 323-227.

13.Design, synthesis and biological evaluation of some novel 3-cinnamoyl-4-hydroxy-2H-chromen-2-ones as antimalarial agents. Kuldeep Patel, Chandrabose Karthikeyan, N. S. Hari Narayana Moorthy, Girdhar Singh Deora, Viswas Raja Solomon, Hoyun Lee , Piyush Trivedi. *Medicinal Chemistry Research* DOI: 10.1007/s00044-011-9694.

14. Development and validation of stability indicating assay method for naratriptan by ultra performance liquid chromatography. Kuldeep Patel, Sunil Singh, Praveen Sahu, Piyush Trivedi. Der Pharmacia Lettre, 2011, 3 (6):102-107

15. Stability indicating HPTLC method for simultaneous determination of valsartan and hydrochlorothiazide in tablets. Sunil singh, kuldeep patel, vipin ku. Agrawal and shashank chaturvedi. *International Journal of Pharmacy and Pharmaceutical Sciences,2012,* Vol 4, Suppl 4,1-4.

16. Simultaneous estimation of S(-) Amlodipine Besylate Hemipentahydrate and Losartan Potassium in Combined Dosage Form by Using UV-Spectroscopy. Sunil Singh, Kuldeep Patel,Vipin Ku. Agrawal, Shashank Chaturvedi, Der Pharmacia Lettre, 2012, 4 (3):897-905.