ISSN: 0975-766X
CODEN: IJPTFI
Available Online through *Research Article*
www.ijptonline.com

ESTIMATION AND VALIDATION OF UV-VISIBLE SPECTROPHOTOMETRIC METHOD FOR COMBINED TABLET DOSAGE FORM OF PARACETAMOL AND DICLOFENAC SODIUM USING EXTRACTIONTECHNIQUE

Sindhu Beeravolu*, Ravi Kumar Vejendla, Sandeep Kumar Nagula
Sri Indu Institute of Pharmacy, Ibrahimpatnam, Ranga Reddy, Andhra Pradesh-501510, India.
Email:sindhubeeravolu@gmail.com

Received on 03-09-2012 *Accepted on 18-09-2012*

Abstract:

Anovel, safe and sensitive method of spectrophotometric estimation inUV-visible region has been developed using 0.1N HCl, 0.1NNaOH for the quantitative determination of DCS and PC.DCS have λmax at 225nm and obeys Beer's law in concentration range of 5-35µg/ml .PC have λmax at 244nm and obey Beer's law in concentration range of 5-35µg/ml.All the results, parameters of the analysis were validated statistically.

Key words: Diclofenac sodium, Extraction Technique, 0.1N HCl, 0.1N NaOH, Paracetamol.

Introduction

The principle behind estimation of Paracetamol and Diclofenac Sodium solution in combined formulation is, each component can be separated by solvent extraction technique[1],[2],[3],[4],[5],[6],[7],[8] that is Paracetamol can be extracted with 0.1N HCl solution and after filtration, the filtrate can be used for Paracetamol estimation and the residue can be used for estimation of Diclofenac Sodium with the help of 0.1N NaoH.Chemically Diclofenac Sodium is sodium[2-(2,6-dichloroanilino)phenyl] acetate, used as analgesic and anti-inflammatory drug. Paracetamol chemically is, N-acetyl-p-aminophenol used as an analgesic and antipyretic. Fixed dose combinations containing Diclofenac Sodium and Paracetamol are available in tablet dosage forms. However, no method has been reported for simultaneous estimation of these two drugs using extractive technique. Hence the present work was attempted to develop accurate, simple and sensitive method for simultaneous estimation[9],[10],[11] of Diclofenac Sodium and Paracetamol using 0.1N NaOH and

0.1N HCl respectively. Therefore it was thought worthwhile to employ this extractive technique to extract out the drug from fine powder of tablets to carry out spectrophotometric estimation.

Experimental

UV/Visible spectrophotometer (Systronics model 2202) was employed with a pair of 1cm matched quartz cell with automatic wavelength correction. Analytical grade reagents and solvents were used for the study; Combined Diclofenac Sodium and Paracetamoltablets (Brand Name-ANAIDA) were procured from the local market.0.1N HCl and 0.1N NaOH was used for further dilutions, obtained from MOLYCHEM. Double distilled water was used for making 0.1N HCl and 0.1 N NaOH.

Preparation of standard and stock solutions

A standard stock solution of 1000µg/ml of Diclofenac Sodium and Paracetamol was prepared by weighing a quantity of powder equivalent to 100mg of Paracetamol from the fine tablet powder containing both PC and DCS.Then the drug is extracted with three portions of 20-25 ml of 0.1N HCl and Whatmann filter paper no.41.First few ml are rejected and combine all the three filtrates and make volume to 100ml with 0.1N HCl. Then take 10ml and dilute to 100ml with o.1N HCl to get 100µg/ml concentration and then further take 20ml from above solution and dilute to 100ml with 0.1NHCl .

to get a concentration of 20µg/ml.Theλmax was measured at 244nm using 0.1N HCl as blank. The entire residue left after extraction of Paracetamol on the filter paper is transferred to 100ml volumetric flask with the help of 0.1N NaOH and make up the volume to 100ml with 0.1N NaOH. Take 10ml of this solution of DiclofenacSodium and dilute to 100ml with 0.1NaOH to get a concentration of 100µg/ml and from the above solution further take 20ml and dilute to 100ml with 0.1NaOH to get a concentration of 20µg/ml and the absorbance of sample solution was measured at 225nm using 0.1N NaOH as blank.

The standard solution of Paracetamol was prepared by crushing 10 tablets and weigh 100mg of Paracetamol powder and dissolve in 50ml of 0.1N HCl and make up volume to 100ml by 0.1N HCl and take 10ml of the above solution and dilute to 100ml with 0.1N HCl and to get 10µg/ml concentration take 10ml from the above and dilute to 100ml with 0.1N HCl. Theabsorbance was measured at 244nm using 0.1N HCl as blank.

The standard solution of DCS was prepared by crushing 10tablets and weigh 100mg of DCS powder and dissolve in 50ml of 0.1N and make up volume to 100ml by 0.1N NaOH and take 10ml of the above solution and dilute to 100ml with 0.1N NaOH and to get 10µg/ml concentration take 10ml from the above and dilute to 100ml with 0.1N NaOH. The absorbance was measured at 225nm using 0.1N NaOH as blank. Five mixed standard solutions with concentrations of PC and DCS in µg/ml of 5:35, 10:30, 15:25, 20:20, 25:15, 30:10, 35:5 overlain spectra of PC and DCS were scanned.

Simultaneous Equation Method

This method of analysis was based on the absorption of drugs (DCS and PC) at the wavelength maximum of the each other [12]. Three wavelengths selected for the development of the simultaneous equations were 225nm, 244 nm; λ max of all two drugs respectively. The absorptivity values E (1%, 1cm) were determined for three drugs at all selected wavelengths.

The concentration of two drugs in mixture was calculated by using following equations.

$$C_{PC} = \frac{A2ay1 - A_1ay_2}{ax_2ay_1 - ax_1ay_2} \quad \text{eq 1}$$

$$C_{DCS} = \frac{A_1ax_2 - A_2ax_1}{ax_2ay_1 - ax_1ay_2} \quad \text{eq 2}$$

Where, *C* DCS and *C*PC are the concentration of PC and DCS respectively in mixture and in sample solutions. A1 and A2 are the absorbances of sample at 244 nm and 225 nm respectively. ax1 and ax2 are the absorptivityof PC at 244 nm and 225 nm respectively. ay1and ay2 are the absorptivity of DCS at 225 nm and 244 nm respectively. Mixed standard solutions of DCS and PC in the ratio of 5:35, 10:30, 15:25, 20:20, 25:15, 30:10, and 35:5 µg/ml were prepared from standard solutions whose volume was made with distilled water and absorbance were measured at 225 nm and 244 nm. Also their respective blanks of 0.1N NaOH and 0.1N HCl solutions were prepared respectively.

CPC = ((A2*220) – (A1*221)) /-45100……eq 1

CDCS = ((A1*230) – (A2*231)) /-45100……..eq 2 (substituting values given in table 1 and 2)

Table-1: Absorbance of Standard and Sample Drugs.

S.NO	Drug	Std abs at 244nm	Std abs at225nm	Sample absorbance
1.	Paracetamol	0.231(x1)	0.230(x2)	0.450(A1)
2.	Diclofenac sodium	0.220(y1)	0.221(y2)	0.450(A2)

Std abs-standard absorbance

Table-2: Absorptivity Values of Standard Drugs

S.NO	DRUG	ABSORPTIVITY at 244nm	ABSORPTIVITY at 225nm
1.	Paracetamol	231×10^2(ax1)	230×10^2(ax2)
2.	Diclofenac sodium	220×10^2(ay1)	221×10^2(ay2)

Results

The mean percent drug estimated in tablet was 99.7±0.210 for Paracetamol and 99.7±0.210 for Diclofenac (table-3). These values are close to 102 indicating the accuracy of proposed analytical method.

Table-3: Results of Tablet Analysis.

DRUG	LABEL CLAIM mg/tab	AMOUNT FOUND* mg/tab	%LABEL CLAIM ±SD	%RSD
Paracetamol	500	498.50	99.7±0.210	0.210
Diclofenac sodium	50	49.85	99.7±0.210	0.210

SD-Standard Deviation, RSD-Relative Standard Deviation,* is mean of 6 estimations.

Validation of Proposed Analytical Method

The method was validated in terms of linearity, accuracy and precision .Recovery studies was performed at three levels on pre-analyzed powder using the same proposed method. Precision study was conducted on interday and intraday

precision study. Linearity of the method was determined by serially diluting the stock solutions to give different concentrations.Caliberation curves were plotted and the drugs showed linearity in the range of 5-35µg/ml for PC and5-35µg/ml for DCS with correlation coefficient 0.999 for each drug.

Validation of the Developed Methods

The developed methods for simultaneous estimation of DCS and PC were validated as per ICH guidelines.

Accuracy

To check the accuracy of the developed methods to study the interference of formulation additives, analytical recovery experiments was carried out by standard addition [13] method. From that total amount of drug found and percentage recovery was calculated.

Repeatability

To check the degree of repeatability of the methods, suitable statistical evaluation was carried out. Five samples of the tablet formulations were analyzed for the repeatability study. The standard deviation, coefficient of variance and standard error was calculated.

Intermediate Precision (Inter-Day and Intra-Day Precision)

The intra and inter-day precision was calculated by assay of the sample solution on the same day and on different days at different time intervals respectively (table-4).

Table-4: Intraday, Interdays, Lod and Loq Data of Tablet Formulation.

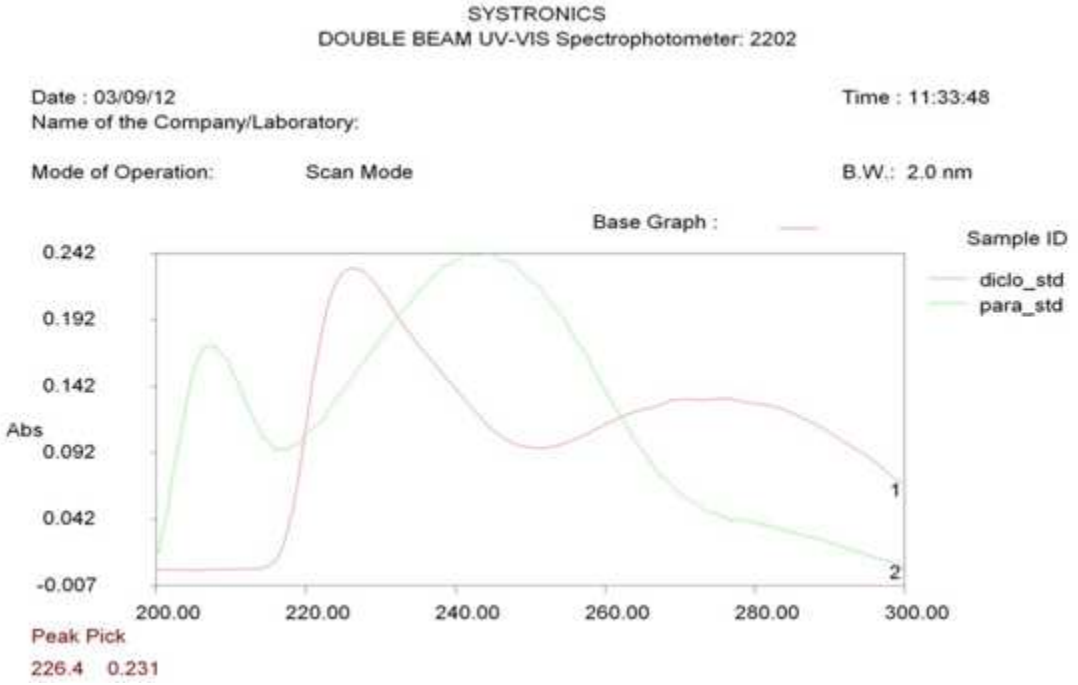
S.NO	**DRUG**	**INTRADAY PRECISION%COV(n=6)**	**INTERDAY PRECISION % COV**		
			Day 1[a]	**Day 2[a]**	**Day 3[a]**
1.	Paracetamol	0.162	0.195	0.220	0.128
2.	Diclofenac Sodium	0.052	0.451	0.125	0.061

[a]Mean of five determinations, COV: Coefficient of variance

Table-5: Result of Tablet Dosage Form Containing Pc and DCS.

PARAMETERS	**METHOD**	
	DCS	PC
Label claim(mg/tab)	50	500
Found(mg/tab)	49.85	498.50
Drug content[a]	100.11	100.51
±S.D	0.210	0.210
%COV	0.189	0.189
SE	0.221	0.316

[a]Value for drug content (%) is the mean of six estimation, Method-Simultaneous equation S.D: Standard deviation, COV: Coefficient of variance and S.E: Standard error.



Analysis of Combined Dosage Form

The absorbance of final sample solution was measured against 0.1N NaOH blank for DCS and 0.1N HCl blank for PC at 225nm and 244nm respectively. The amount of DCS and PC was computed by adding the absorbance value in simultaneous equation.

Recovery Studies

The method was validated by recovery study were carried out by addition of different amount of drugs to pre analyze solution (10µg/ml).From the stock solution of 100µg/ml of each drug 1ml solution was taken in each of four volumetric flask (10ml), then 1.2, 0.8, 0.4 ml of mixed standard stock solution (100µg/ml of DCS and 100µg/ml of PC) added in three flasks so that remaining one flask contains no added solution. These solutions were scanned at 225nm and 244nm respectively. Percentage recovery was found to be in the range of 99.5 to 102.5%.

Conclusion and Discussion

The proposed method was validated as per ICH guidelines. The mean percent drug estimated in tablet was 99.7±0.310 for Paracetamol and 99.7±0.310 for Diclofenac. These values are close to 102.5% indicating the accuracy of proposed analytical method. %RSD were found to be less than 2.The low values of these statistical parameters validated the method.LOD and LOQ were found to be 0.195, 0.220, 0.128 for DCS and 0.451, 0.125, 0.061 for PC respectively. The %recovery was found to be 99.7-102% and 99.7-102.3% for DCS and PC respectively which indicate the method has required accuracy. Interday and Intraday precision studies showed that %RSD values <1% that signifies the precision of the method. There was no interference from the common excipients present in the tablet and also of the extractive agents 0.1N HCl and 0.1N NaOH used in the analysis. Thus it may be concluded that the proposed method is new, simple, precise and cost-effective.

Acknowledgement

The authors are thankful to Principal Sri Indu institute of Pharmacy (A.P) for providing pure drug samples and other facilities.

References

1. Maheshwari R.K, *The Indian Pharmacist*, 36**,** 63-68, (2005).

2. Maheshwari R.K, Chaturvedi S.C. and Jain N.K, *Indian Drugs*, 42(8)**,** 541-544, (2005).

3. Maheshwari R.K, *Asian J. Chem*, 18(1),393-396,(2006).

4. Maheshwari R.K, *Asian J. Chem*, 18(1),640-644,(2006).

5. Maheshwari R.K, and Bhatt P, *Asian J. Chem*, 18(2), 1481-1486,(2006).

6. Maheshwari R.K, and Pandey S.P, *Asian J. Chem*,18(2),1451-1454,(2006).

7. Maheshwari R.K, *Asian J. Chem*, 18(4), 3194-3196,(2006).

8. Maheshwari R.K, *Indian Journal ofPharmaceutical Education and Research*, 40(4)237-240, (2006)

9. Maheshwari R.K, and Dewangan A, *Asian J.Chem*, 18(4), 2879-2882, (2006).

10. Maheshwari R.K, *The Indian Pharmacist*, 5(50), 87-90, (2006).

11. Maheshwari R.K, Chavda V, Sahoo K, and Varghese S, *Asian J. Pharmaceutics*, 1, 30-32, (2006).

12. Davison A G, Beckette A H, StenlakeJ.B, *Practical Pharmaceutical Chemistry*, CBS Publishers and distributors, New Delhi., 1997,275.

13. *ICH Q2B:* Text on Validation of AnalyticalProcedures-Methodology Step 4, Consensus Guidelines, ICH Harmonized TripartiteGuidelines, 1996.

Corresponding Author:

Sindhu Beeravolu*,

Email:*sindhubeeravolu@gmail.com*