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Determination and Validation of UV-Spectrophotometric method for Estimation of Paracetamol and Diclofenac Sodium in Tablet Dosage Forms Using Hydrotropic Solubilizing Agents

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Abstract: A novel, safe and sensitive method of spectrophotometric estimation in UV-region has been developed using 5 M urea solution as hydrotropic solubilizing agent for the quantitative determination of DCS and PC (Poorly water soluble drugs in tablet dosage form). DCS have λ_{max} at 261.1 nm and obeys Beer's law in concentration range of 5-35 µg/ml. PC have λ_{max} at 247.8 nm and obeys beer's law in concentration range of 5-35 µg/ml. Urea solution does not shows any absorption above 236 nm and does not show any interference in spectrophotometric estimations. All the results, parameters of the analysis were validated statistically.

Key words: *Diclofenac sodium, Paracetamol, Urea, Hydrotropic Solubilization Technique.*

Introduction

The term "HYDROTROPY" has been used to designate the increase in solubility of various substances due to the presence of large amounts of additives. Various hydrotropic agents have been used to enhance the aqueous solubility of a large number of drugs.[1], [2], [3] ,[4], [5], [6] [7], [8]. Sodium salicylate, urea, nicotinamide, sodium ascorbate and sodium citrate are the popular examples of hydrotropic agents. Various organic solvents such as urea, chloroform and dimethyl formamide have been employed for solubilization of poor water soluble drugs to carry out spectrophotometric analysis. Drawbacks of organic solvents include their higher cost, toxicity and pollution. Hydrotropic solution may be a proper choice to preclude the use of organic solvents. 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 analgesic and antipyretic. Fixed dose combinations containing diclofenac sodium and paracetamol available in tablet dosage forms. Diclofenac sodium and paracetamol alone has been reported to be estimated by using hydrotropic agents [9], [10], [11].However, no method has been reported for simultaneous estimation on combination of these two drugs in tablet dosage form. Hence, the present work was attempted to develop accurate, simple and sensitive method for simultaneous estimation of diclofenac sodium and paracetamol in tablet dosage forms using 5 M urea solution. In the preliminary solubility studies, there was more than 28 and 22 folds enhancement in the solubility of diclofenac sodium and paracetamol in 5 M urea solution. Therefore, it was thought worthwhile to employ this hydrotropic solution to extract out the

drug from fine powder of tablets to carry out spectrophotometric estimation.

Experimental

UV/Visible spectrophotometer (Shimadzu Model 1601) was employed with spectral bandwidth of 1 nm and wavelength accuracy of 0.3 nm (with automatic wavelength correction with a pair of 1 cm matched quartz cells). Analytical grade reagents and solvents were used for the study; Combined diclofenac sodium and paracetamol tablets were procured from the local market. 5 M urea solution was used to solublize the drugs and distilled water was used for further dilutions.

Preparation of standard and sample solution:

A standard stock solution of 1000µg/ml of diclofenac sodium and paracetamol were prepared by taking 50 mg of each drug in 50 ml volumetric flask and was dissolved in 20 ml of 5M urea solution and then further volume was made with distilled water. From the standard stock solutions, aliquot portions were suitably diluted to different concentrations and linearity was studied. From these stock solutions, working standard solutions were prepared by appropriate dilution of aliquot portions with the solvent to get final concentration of 20 µg/ml of each and were scanned in the wavelength range of 400-200 nm to determine λ_{max}. The overlain zero order spectra of diclofenac sodium and paracetamol indicate 261.1 nm and 247.8 nm as absorption maxima (λ_{max}) of DCS and PC respectively and isobestric point as 283.9 nm. The stock solution was prepared by dissolving 100 mg of DCS in 75 ml of Urea in 100 ml volumetric flask, shaken and the volume was made up to the mark with Urea,10 ml of this solution was diluted up to 100 ml with Urea in another volumetric flask produce final stock solution of 100 µg/ml of DCS. Standard stock solution of PC was prepared similarly as that of DCS. The sample solution was then filtered through Whatmann filter paper no 41 and first few ml were rejected. From two solutions, 1 ml of the solution was taken and diluted to 10 ml to get a stock solution containing 100 µg/ml of DCS and corresponding concentration of PC. Beer-Lambert's law was found to be obeying in the concentration range of 5-35 µg/ml for both the drugs in all the three methods. For method A and B five mixed standards solutions with concentration of DCS and PC in µg/ml of 5:35,10:30,15:25,20:20,25:15,30:10,35:5 Overlain spectra of DCS and PC were scanned . Ten tablets were weighed and crushed to fine powder. The powder sample equivalent to 50 mg of DCS and 325 mg of PC was weighed and transferred to 50 mL of volumetric flask and dissolved in 20 mL of 8M urea solution with frequent shaking for 15 minutes. Finally the volume was made up to the mark with distilled water. The solution was filtered through Whatmann filter paper No. 41. Appropriate dilutions were made to get the concentration as 5 µg/ml of DCS and 15 µg/ml of PC and absorbances were measured at 261.1 nm and 247.8 nm. The concentration of DCS and PC were obtained from the equation 1 and 2. The result of tablet analysis is given in table.

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 261.1 nm, 247.8 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.

$$C_{DCS} = \frac{A_2 a y_1 - A_1 a y_2}{a x_2 . a y_1 - a x_1 a y_2} \quad \text{.... (1)}$$

$$C_{PC} = \frac{A_1 a x_2 - A_2 a x_1}{a x_2 . a y_1 - a x_1 a y_2} \quad \text{..... (2)}$$

Where, C_{DCS} and C_{PC} are the concentration of DCS and PC respectively in mixture and in sample solutions. A_1 and A_2 are the absorbances of sample at 261.1 nm and 247.8 nm respectively. ax_1 and ax_2 are the absorptivity of DCS at 261.1 nm and 247.8 nm respectively. ay_1 and ay_2 are the absorptivity of PC at 261.1 nm and 247.8 nm respectively. Mixed standard solutions of DCS and PC in the ratio of 5:35,10:30,15:25,20:20,25:15,30:10,35:5 µg/ml were prepared from standard solutions whose volume was made with distilled water and absorbance were measured at 261.1 nm and 247.8 nm. Also their respective blanks of 5 M urea solutions were prepared.

$C_{PC} = ((A_2 * 102.15) - (A_1 * 264.87)) / -16542$……eq 1

$C_{DCS} = ((A_1 * 221.62) - (A_2 * 541.95)) / -16542$……..eq 2

Validation of the proposed method

The method was validated in terms of linearity, accuracy and precision. Recovery study was performed at three levels on pre-analyzed powder using the same proposed method. Precision study was conducted as intraday and interday precision study. Linearity of the method was determined by serially diluting the stock solutions to give different concentrations. Calibration

curves were plotted and the drugs showed the linearity in the range of 5-20 µg/ml for PC and 5-40 µg/ml for DCS with correlation coefficient of 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 and to study the interference of formulation additives, analytical recovery experiments was carried out by standard addition method [13]. From that total amount of drug found and percentage recovery was calculated.

Precision

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. The results are presented in Table 2.

Analysis of combined dosage form

The absorbance of final sample solution was measured against methanol as blank at 261.1 and 247.8 nm. 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 the 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 261.1nm and 247.8 nm. Percentage recovery was found in the range of 100 % to 105%.

Table no. 1- Result of tablet analysis

Drug	Label claim mg/tab	Amount found* mg/tab	% Label claim ± SD	% RSD
DCS	50	51.12	100.04 ± 0.211	0.212
PC	325	325.08	103.75 ± 0.117	0.118

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

Table 2. Intraday, Interdays, LOD and LOQ data of tablet formulation.

Method	Drug	Intra day precision %COV (n=6)	Interday precision %COV		
			Day 1[a]	Day 2[a]	Day 3[a]
Method	DCS	0.162	0.195	0.220	0.128
	PC	0.052	0.451	0.125	0.061

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

Table 3. Result of tablet dosage form containing DCS and PC.

Parameters	Method	
	DCS	PC
Label claim (mg/Tab)	50	325
Found (mg/Tab)	50.11	325.15
Drug content[a]	100.11	100.51
±S.D	0.251	0.164
%COV	0.189	0.155
SE	0.221	0.316

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

Result and Discussion

The proposed method was validated as per the ICH guidelines. The mean percentage drug estimated in tablet form was 100.04 ± 0.211 for DCS and 103.75 ± 0.117 for PC. These values are close to 105.12, indicating the accuracy of the proposed analytical method. % RSD values were found to be less than 5. The low values of these statistical parameters validated the method. LOD and LOQ were found to be 0.195, 0.220, and 0.128 for DCS and 0.451, 0.125, 0.061 for PC respectively. The % recovery for DCS was from 100.03-101.67 % and for PC was 100.32-103.97 % which indicate that method has required accuracy. Interday and intraday precision studies showed % 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 hydrotropic agent, urea, used in the analysis. Thus, it may be concluded that the proposed method is new, simple, eco-friendly (precluding the use of organic solvents), precise, and cost-effective.

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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 of Pharmaceutical 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, Stenlake J.B, *Practical Pharmaceutical Chemistry*,CBS Publishers and distributors, New Delhi., 1997, 275.
13. *ICH Q2B:* Text on Validation of Analytical Procedures-Methodology Step 4, Consensus Guidelines, ICH Harmonized Tripartite Guidelines, 1996.

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