VALIDATED SIMULTANEOUS SPECTRO PHOTOMETRIC METHOD FOR ESTIMATION OF PARACETAMOL & DICLOFENAC SODIUM IN TABLET DOSAGE FORMS USING HYDROTROPIC SOLUBILIZATION TECHNIQUE

Engla G[1]., Doshi A[1]., Soni. L.K.[1] and Dixit V.K.[2]

[1] GRY Institute of Pharmacy, Borawan (M.P.), [2] Dr. H.S. Gaur University of Pharma Science, Sagar (M.P.)

Abstract

A novel, safe and sensitive method of spectrophotometric estimation in UV- region has been developed using 8M urea solution as hydrotropic solubilizing agent for the quantitative determination of DCS and PC . A poorly water soluble drugs in tablet dosage form. DCS have maximum λmax at 275.6 nm and obeys Beer's law in concentration range of 5-40 μg/ml. PC have λmax at 243.4 nm and obeys beer's law in concentration range of 5-20 μg/ml. Urea solution does not absorbs above 244 nm and does not show any interference in spectrophotometric estimation. Results of the analysis were validated statistically.

Key words: Diclofenac sodium, Paracetamol, Urea.

Introduction:

The term "hydrotopy" 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 methanol, chloroform and dimethyl formamide have been employed for solubization of poorly water soluble drug 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 market in tablet form. 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 8M urea solution.

In the preliminary solubility studies, there was more than 28 and 22 folds enhancement in the

*Address for Correspondence

Gajanand Engla

GRY Institute of Pharmacy, Borawan (M.P.), e-mail : gajanand54@gmail.com

solubility of diclofenac sodium and paracetamol in 8M urea solution. Therefore, it was thought worthwhile to employ this hydrotropic solution to extract out the drug from from fine powder of tablets to carry out spectrophotometric estimation.

Experimental

A Shimadzu-1700 double beam UV spectrophotometer, with a pair of 10.0mm matched quartz cell was employed for spectrophotometric analysis. Pure drug samples of diclofenac sodium and paracetamol were obtained from GRY Institute of Pharmacy, Borawan. Combined diclofenac sodium and paracetamol tablets were procured from the local market. 8M urea solution was used to solublize the drugs and distilled water was used for further dilutions.

Standard stock solutions of 1000*µg*/ml of diclofenac sodium and paracetamol were prepared by taking 50mg of each drug in 50ml volumetric flask and was dissolved in 20ml of 8M 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 λmax. The overlain zero order spectra (fig.1) of diclofenac sodium and paracetamol indicate 275.6 nm and 243.4 nm as absorption maxima (λmax) of disclofenac Sodium and paracetamol respectively and isobestic point as 264.0 nm.

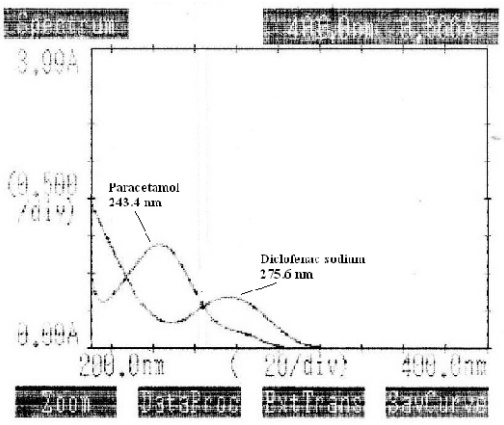

FIG.1 - Overlain zero order spectra of paracetamol and diclofenac sodium

Mixed standard solutions of dcs and pc in the ratio of 5:20, 10:15, 15:10, 20:5 *µg*/ml were prepared from standard solutions whose volume was made with distilled water and absorbance were measured at 275.6 nm and 243.4 nm. Also their respective blanks of 8M urea solutions was prepared.

The absorbance and absorptivity values at the particular wavelengths were substituted in the simultaneous equation :

CPC = (A2ay1 – A1ay2) / (ax2ay1 – ax1ay2)

CDCS = (A1ax2 – A2ax1) / (ax2ay1 – ax1ay2)

Where,

A1 & A2 are absorbance of the sample at 243.4 nm & 275.6 nm.

ax1 & ay1 are absorptivities of PC and DCS at 243.4 nm.

ax2 and ay2 are absorptivities of PC and DCS at 275.6 nm.

After substituting the absorptivity values the equation obtained was as

CPC = ((A2*193.98) – (A1*350.56)) / -213176……eq 1

CDCS = ((A1*135.25) – (A2*689.70)) / -213176……..eq 2

Twenty 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 2μg/ml of DCS and 13 μg/ml of PC and absorbances were measured at 275.6 nm and 243.4 nm. The concentration of DCS and PC were obtained from the equation 1 and 2. The result of tablet analysis is given in table 1.

Drug	Label claim mg/tab	Amount found* mg/tab	% Label claim ± SD	% RSD
DCS	50	50.02	100.04 ± 0.386	0.385
PC	325	325.68	100.21 ± 0.196	0.195

Table no. 1- Result of tablet analysis

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

Validation of the proposed method:

The method was validated in terms of linearity, accuracy and precision. Recovery study was performed at three levels on preanalyzed powder using the same proposed method. Precision study was conducted as intraday and interlay 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.

Result and Discussion:

The proposed method was validated as per the ICH guidelines. The mean percent drug estimated in tablet form was 100.04 ± 0.386 for DCS and 100.21 ± 0.196 for PC. These values are close to 100, indicating the accuracy of the proposed analytical method. % RSD values were found to be less than 2. The low values of these statistical parameters validated the method.

LOD and LOQ were found to be 0.1431, 0.2746 for DCS and 0.0316, 0.2547 for PC respectively. The % recovery for DCS was from 99.03-101.67 % and for PC was from 98.35-100.97 % which indicate that method has required accuracy. Interday and intraday precision studies showed % RSD values <

2% 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. Therefore, a large number of poorly water-soluble drugs having λmax above 244 nm may be tried for estimation by this method, provided their solubility are enhanced sufficiently by urea solution as urea shows no absorbance above 244 nm.

Acknowledgement

The authors are thankful to Principal, GRY Institute of Pharmacy, Borawan for providing pure drug samples and other facilities.

References

1. Maheshwari R.K. Spectrophotometric determination of cefixime in tablets by hydrotropic solubilization phenomenon. *The Indian Pharmacist.* 4 (36); 2005: 63-68.
2. Maheshwari R.K., Chaturvedi S.C. & Jain N.K. Application of hydrotropic solubilization phenomenon in spectrophotometric analysis of hydrochlorothiazide tablets. *Indian Drugs.* 42(8); 2005: 541-544.
3. Maheshwari R.K. A Novel Application of Hydrotropic Solubilization in the Analysis of Bulk Samples of Ketoprofen and Salicylic Acid. *Asian J. Chem.*, 18(1); 2006: 393-396.
4. Maheshwari R.K. Novel Application of Hydrotropic Solubilization in the Sectrophotometric Analysis of Tinidazole in Dosage Form. *Asian J. Chem.* 18(1); 2006: 640-644.
5. Maheshwari R.K., Maheshwari R.B., Bhatt P. Simultaneous estimation of norfloxacn and tinidazole in two component tablet formulation. *Asian J. Chem.* 18(2); 2006: 1481-1486.
6. Maheshwari R.K., Pandey S.P., Lovelaker A., Chavda V., Ajmera A. Novel application of hydrotropic solubilization in the spectrophotometric analysis of Cephalexin in solid dosage form. *Asian J. Chem.* 18(2); 2006 1451-1454.
7. Maheshwari R.K. Spectrophotometric Analysis of Amoxycillin in Tablets Using Hydrotropic Solubilization Technique. *Asian J. Chem.* 18(4); 2006: 3194-3196.
8. Maheshwari R.K. Application of hydrotropic solubilization phenomenon in spectrophotometric estimation of norfloxacin in tablets. *Indian Journal of Pharmaceutical Education and Research.* 40(4); 2006: 237-240.
9. Maheshwari R.K., Dewangan A., Soni P.K., Jain S.K. Novel application of hydrotropic solubilization in the spectrophotometric analysis of paracetamol tablet. *Asian J. Chem.*, 18(4); 2006: 2879-2882.
10. Maheshwari R.K., Solid dispersion and syrup formulation of poorly water soluble drugs by hydrotrophy. *The Indian Pharmacist.* 5(50); 2006: 87-90.
11. Maheshwari R.K., Chavda V., Sahoo K., Varghese S., Novel application of hydrotropic solubilization in the spectrophotometric analysis of diclofenac sodium in solid dosage form. *Asian J. Pharmaceutics.* 1; 2006: 30-32.