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Research Article

# Method Development and Validation for Simultaneous Estimation of Cefpodoxime Proxetil and Dicloxacillin Sodium by Hydrotropy Using UV Spectroscopy

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**ABSTRACT**

The present work describes the development of accurate, precise and high economic value for the simultaneous estimation of Cefpodoxime proxetil and Dicloxacillin sodium by hydrotropy method using UV spectroscopy was developed and validated. The method was performed on Lab India, model UV-3000 spectrophotometer with UV win software. 1M urea was used as a solvent for analysis. Detection was carried out at 230nm for Cefpodoxime proxetil and 210 nm for Dicloxacillin sodium. Linearity was observed at concentration range 2-20 µg/ml for Cefpodoxime proxetil and 5-30 µg/ml for Dicloxacillin sodium. Correlation coefficient for Cefpodoxime proxetil and Dicloxacillin sodium was found to be 0.993 and 0.9998 respectively. The method can be successfully applicable to routine analysis.

Keywords: Cefpodoxime proxetil, Dicloxacillin sodium, 1M urea solution, Hydrotropy.

## INTRODUCTION

Hydrotropy is a phenomenon in which solubility of poorly water soluble and water insoluble drugs can be increased by addition of some anionic organic salts which are commonly called as Hydrotropic agents/ Hydrotropes. The mechanism by which it improves solubility is closely related to complexation involving weak interaction between the hydrotropic agents like Benzoic acid, Salicylic acid, Urea etc[1-3].

Cefpodoxime proxetil is third generation Cephalosporin antibiotic. Chemically it is (7R)-7-{[2Z)-2-(2-amino-1,3-thiazol-4-yl)methoxyiminoacetyl]amino}-3-methoxymethyl)-8-oxo-5-thia-1-azabicyclo[4.2.0]2-oct-2-enecarboxylicacid (Fig-1). It is active against wide spectrum of Gram positive and Gram negative bacteria. Cefpodoxime is inactivated by certain extended spectrum inhibition of cell wall synthesis. The active metabolite of cefpodoxime binds preferentially to binding protein3, which inhibits production of peptidoglycan, the primary constituent of bacterial cell wall[4-6].

Dicloxacillin sodium is penicillin derivative antibacterial drug which is resistant to penicillinase. Chemically it is (2S,5R,6R)-6-{[3-(2,6-dichlorophenyl)-5-methyloxazole-4-carbonyl]amino}-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptanes-2-carboxylicacid (Fig-2). It acts by inhibiting the synthesis of bacterial cell wall. It inhibits cross linkage between the linear peptidoglycan polymer chains that make up a major component of the cell wall of gram positive bacteria[7,8].

## MATERIALS AND METHODS

*Instrument*

A Lab India UV/Visible double beam spectrophotometer model UV 3000 with software UV win was used for this method.

*Chemical*

Cefpodoxime proxetil (CFPX), Dicloxacillin sodium (DCLX) bulk powder was kindly gifted by Acme pharmaceuticals Ltd., Ahmedabad, India. Combined tablet formulations were procured from local market. All chemicals and reagents used were of analytical grade and purchased from Ranbaxy fine chemicals Ltd.

*Preparation of 1M urea solution (Hydrotropic agent)*

60g of urea was accurately weighed and taken into 1000ml volumetric flask and 500ml of water was added. The solution was shaken well until the solid dissolves. Then the volume was made up to 1000ml with distilled water to give 1M solution. This was further used as solvent and also as blank.

*Preparation of standard stock solution*

10mg of cefpodoxime proxetil and Dicloxacillin sodium were accurately weighed and taken in 100ml volumetric flask separately and make up the volume with 1M urea which gives final strength about 100µg/ml.

*Selection of wavelength*

Take appropriate volume of Cefpodoxime proxetil and Dicloxacillin sodium of about 10ml and 5ml respectively in 100ml volumetric flask and make up the volume with 0.1M urea. Scan the resulting solution in UV range (200-400nm). In the spectrum of Cefpodoxime proxetil and Dicloxacillin sodium 230nm and 210nm respectively is selected for simultaneous estimation.

*Selection of analytical concentration*

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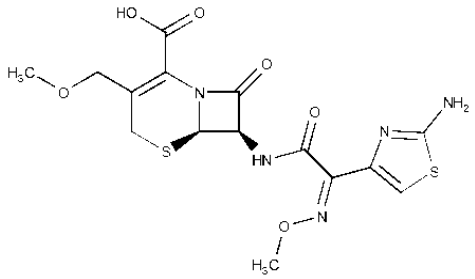

Figure 1: Structure of Cefpodoxime proxetil

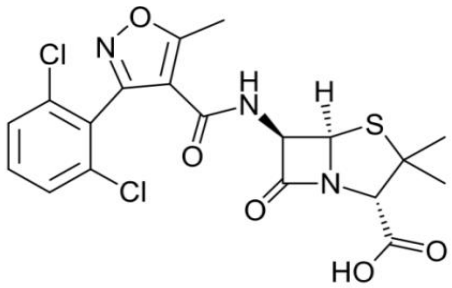

Figure 2: Structure of Dicloxacillin sodium

Table 1: Linearity results of CFPX and DCLX.

| Concentartion of CFPX (µg/ml) | Absorbance of CFPX | Concentartion of DCLX (µg/ml) | Absorbance of DCLX |
|---|---|---|---|
| 2 | 0.051 | 5 | 0.419 |
| 4 | 0.081 | 10 | 0.786 |
| 8 | 0.165 | 15 | 1.165 |
| 12 | 0.263 | 20 | 1.502 |
| 16 | 0.386 | 25 | 1.887 |
| 20 | 0.465 | 30 | 2.243 |

Table 2: Parameters of CFPX and DLX

| Parameters | CFPX | DCLX |
|---|---|---|
| Linearity range(µg/ml) | 2-20 | 5-30 |
| Correlation coefficient($r^2$) | 0.993 | 0.9998 |
| Slope(m) | 0.0233 | 0.0729 |
| Intercept(c) | -0.0076 | 0.0577 |
| Regression equation | y=mx+c<br>y= absorbance,<br>x= concentration | |

From the standard stock solution of cefpodoxime proxetil, aliquots of 0.2, 0.4, 0.6, 0.8, 1.0ml were taken into a series of five 10ml volumetric flasks. The volume was made up to the mark with water to get solutions having the concentration range 2, 4, 6, 8, 10µg/ml of Cefpodoxime proxetil. Absorbances of the above solutions were measured at 208nm and 230nm.

From standard stock solution of Dicloxacillin sodium, aliquots of 0.5, 1.0, 1.5, 2.0, 2.5ml were taken into a series of five 10ml volumetric flasks. The volume was made up to mark with distilled water to get solutions having the concentration range 5, 10, 15, 20, 25µg/ml of Dicloxacillin sodium. Absorbances of the above solutions were measured at 208nm and 230nm.

*Analysis of commercial formulation*

Twenty tablets were weighed and the average weight was calculated. A quantity of powdered tablets equivalent to 200mg and 500mg of cefpodoxime proxetil and Dicloxacillin sodium was weighed accurately and transferred into 100ml volumetric flask. The solution was diluted to 100ml with 0.1M urea. Then 10ml of the above solution was taken into 100ml volumetric flask and diluted with methanol which gives 200µg/ml of Cefpodoxime proxetil and 500µg/ml of Dicloxacillin sodium. 5ml of the above solution was diluted up to 100ml with methanol which gives 10 µg/ml of cefpodoxime proxetil and 25µg/ml Dicloxacillin sodium in the formulation was determined using the formula of simultaneous equation method.

*Method validation*[9-22]

*Linearity*

From the standard standard stock solution, appropriate aliquots were taken into a series of five 10ml volumetric flasks. The volume was made up to mark with solvent to get solutions having the concentration range 2, 4, 6, 8, 10 and 5, 10, 15, 20, 25µg/ml of Cefpodoxime proxetil and Dicloxacillin sodium respectively. Absorbances of the above solutions were measured at 230nm and 210 nm respectively. Calibration curve was plotted taking concentration on x-axis and absorbance on Y-axis. The results were given in table-1 & 2 and Fig-3.

*Accuracy and Recovery studies*

To check the accuracy of the proposed method, recovery studies were carried out by standard addition method at three different levels according to ICH guidelines. A series of solutions of cefpodoxime proxetil and Dicloxacillin sodium at 80%, 100%, and 120% of the standard preparation in the ratio of the formulation were prepared and checked for accuracy by determining the absorbance values at $\lambda_{max}$ of 230nm and 210nm respectively. To a fixed concentration of the formulation, varying concentration of pure drug solutions was added and percentage recoveries were calculated. The result of the analysis is given in Table-3.

*Precision*

Precision studies were performed at three different concentrations in the ratio of the formulation, each concentration prepared three times for Cefpodoxime proxetil and Dicloxacillin sodium together. The result of the analysis is given in Table-4&5.

## RESULTS AND DISCUSSION

The proposed method for determination of CFPX and DCLX in tablet dosage form was found to be precise, accurate and also has more economic value. The present study describes the method development and validation for simultaneous estimation of CFPX and DCLX in tablet dosage form by hydrotropy using using UV spectroscopy. The $\lambda_{max}$ of CFPX and DCLX were found to be 230nm and 210nm respectively. The linearity was observed in concentration range of 2-20µg/ml of the test concentration

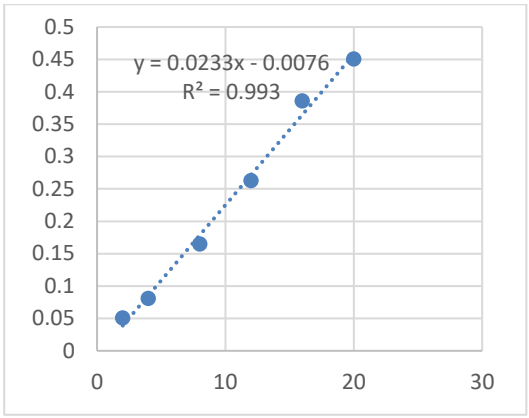


Figure 3a: Linearity graph of CFPX.

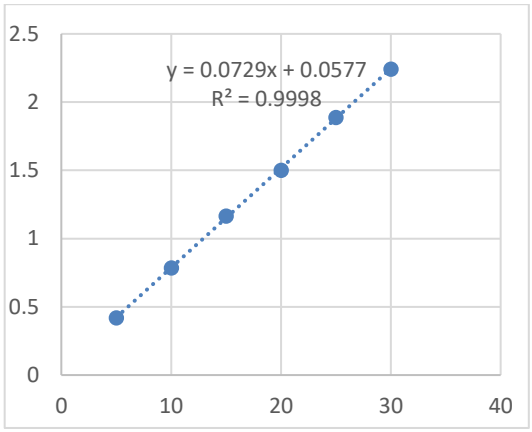


Figure 3b: Linearity graph of DCLX.

Table 3: Accuracy results of CFPX and DCLX.

| Level | Spike (µg/ml) | | Absorbance of spike | | Found conc. | | % recovery | | S. D | | % R.S. D | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | CFPX | DCLX | 230nm | 210nm | CFPX | DCLX | CFPX | DCLX | CFPX | DCLX | CFPX | DCLX |
| 80% | 8 | 20 | 0.172 | 1.511 | 7.708 | 19.935 | 96.35 | 99.675 | | | | |
| | 8 | 20 | 0.169 | 1.508 | 7.579 | 19.894 | 94.73 | 99.470 | 1.544 | 0.201 | 1.632 | 0.202 |
| | 8 | 20 | 0.165 | 1.504 | 7.407 | 19.839 | 92.58 | 99.195 | | | | |
| 100 % | 10 | 25 | 0.225 | 1.887 | 9.982 | 25.093 | 99.82 | 100.37 | | | | |
| | 10 | 25 | 0.223 | 1.885 | 9.896 | 25.065 | 98.96 | 100.26 | 1.086 | 0.219 | 1.101 | 0.278 |
| | 10 | 25 | 0.219 | 1.882 | 9.721 | 25.024 | 97.21 | 100.09 | | | | |
| 120 % | 12 | 30 | 0.269 | 2.249 | 11.871 | 30.058 | 98.92 | 100.19 | | | | |
| | 12 | 30 | 0.265 | 2.247 | 11.699 | 30.031 | 97.49 | 100.10 | 0.894 | 0.114 | 0.915 | 0.114 |
| | 12 | 30 | 0.263 | 2.243 | 11.613 | 29.976 | 96.77 | 99.92 | | | | |

Table 4: Results of Intraday precision of CFPX and DCLX.

| Concentration | | Absorbance | | Found concentration | | % Assay | |
|---|---|---|---|---|---|---|---|
| CFPX | DCLX | CFPX | DCLX | CFPX | DCLX | CFPX | DCLX |
| 100% | 100% | 0.231 | 1.889 | 10.240 | 25.120 | 102.4 | 100.48 |
| 100% | 100% | 0.226 | 1.882 | 10.026 | 25.025 | 100.26 | 100.1 |
| 100% | 100% | 0.225 | 1.887 | 9.982 | 25.093 | 99.82 | 100.37 |
| 100% | 100% | 0.229 | 1.885 | 10.154 | 25.065 | 101.54 | 100.26 |
| 100% | 100% | 0.230 | 1.893 | 10.197 | 25.175 | 101.97 | 100.7 |
| 100% | 100% | 0.229 | 1.886 | 10.154 | 25.079 | 101.54 | 100.31 |
| | | AVERAGE | | | | 101.19 | 100.37 |
| | | SD | | | | 0.338 | 0.755 |
| | | %RSD | | | | 0.334 | 0.752 |

and the correlation coefficient ($r^2$) for the calibration curve was found to be 0.993 for CFPX and concentration range of 5-30µg/ml of the test concentration and the correlation coefficient ($r^2$) for the calibration curve was found to be 0.9998 for DCLX. The results of recovery 92.58-99.82% for CFPX and 99.195-100.37% for DCLX indicating accuracy of the method and good recovery of the drug. The %RSD for tablet analysis is less than 2 which indicate high degree of precision. The assay of the sample shows the drug present within the specification limit indicates the purity of the formulation. Hence it can be concluded that the method of hydrotropy using UV spectroscopy is accurate, precise and also has more economic value. It can be employed successfully for the estimation of CFPX and DCLX in tablet dosage form by hydrotropy method using UV spectroscopy.

## CONCLUSION

A relatively simple, specific and sensitive method was developed for the simultaneous estimation of CFPX and DCLX in tablet dosage forms. The proposed and validated UV spectrophotometric method was highly sensitive, reproducible, accurate, and precise and also has more economic value. The developed method was validated as per ICH (Q2B) guidelines and was found to be applicable for routine quantitative analysis of CFPX and DCLX by

Table 5: Results of Interday precision of CFPX and DCLX.

| Concentration | | Absorbance | | Found concentration | | % Assay | |
|---|---|---|---|---|---|---|---|
| CFPX | DCLX | CFPX | DCLX | CFPX | DCLX | CFPX | DCLX |
| 100% | 100% | 0.231 | 1.889 | 10.240 | 25.120 | 102.4 | 100.48 |
| 100% | 100% | 0.228 | 1.887 | 10.111 | 25.093 | 101.11 | 100.37 |
| 100% | 100% | 0.225 | 1.885 | 9.982 | 25.065 | 99.82 | 100.26 |
| 100% | 100% | 0.223 | 1.883 | 9.896 | 25.038 | 98.96 | 101.15 |
| 100% | 100% | 0.231 | 1.892 | 10.240 | 25.161 | 102.4 | 100.64 |
| 100% | 100% | 0.227 | 1.884 | 10.068 | 25.052 | 100.68 | 100.20 |
| AVERAGE | | | | | | 100.89 | 100.51 |
| | | SD | | | | 0.8 | 0.846 |
| | | %RSD | | | | 0.792 | 0.841 |

UV spectroscopy in dosage forms. The developed and validated UV spectroscopic method was found to be better than previous methods because it is rapid, having high economic value and also environmental friendly procedure that allows the analysis of large number of samples in a short period of time. The method has been found to be better than the previously reported methods due to its high economic value, wide range of linearity, lack of extraction procedures. Hence above method can be used in quality control for routine analysis of tablets of CFPX and DCLX without any interference.

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