AMERICAN JOURNAL OF PHARMTECH RESEARCH

Journal home page: http://www.ajptr.com/

Method Development and Validation of Cefpodoxime Proxetil in Bulk and Pharmaceutical Formulation by Using UV Spectrophotometer.

Most. Umme Bushra[1*], Kazi Rakibul Islam[1], Md. Saddam Hossain[1], Asma Hossain Sarah[1] Md. Anamul Hasan Allied[2]

1Department of Pharmacy, Manarat International University, Mirpur, Dhaka, Bangladesh.
2Department of Pharmacy ,University of Asia pacific, Dhanmondi, Dhaka,Bangladesh

ABSTRACT

The present study was undertaken to develop and validate a simple, accurate, precise, reproducible and cost effective UV-Visible spectrophotometric method for the estimation of cefpodoxime proxetil in bulk and pharmaceutical formulation. The solvent used throughout the experiment was methanol and water. Absorption maximum (λ_{max}) of the drug was found to be 231 nm. The quantitative determination of the drug was carried out at 231 nm and Beer's law was obeyed in the range of 5-25µg/mL. The method was shown linear in the mentioned concentrations having line equation y = 0.0331x + 0.0151 with correlation coefficient $R^2$of 0.9998. The recovery values for cefpodoxime proxetil ranged from 99.80% - 100.02%.The percent relative standard deviation (RSD %) of interday precision range was 0.118 – 0.181% and intraday precision range was 0.139 – 0.446%. The limit of detection and limit of quantification was 0.081µg/mL and 0.121µg/mL. The percent relative standard deviation of robustness and ruggedness of the method was 0.126 – 0.313%.Cefpodoxime proxetil content in two pharmaceutical dosage forms (tablet and suspension) were determine which were in good agreement with the label claims with RSD value of 0.02% for tablet and 0.01% for suspension. Hence, proposed method was precise, accurate and cost effective. This method could be applicable for quantitative determination of the bulk drug as well as dosage formulation.

Keywords: UV-Vis Spectrophotometer, Method Validation, Recovery studies.

*Corresponding Author Email: bushra3march@gmail.com
Received 13 January 2014, Accepted 19 January 2014

Please cite this article in press as: Bushra MU. *et al.*, Method Development and Validation of Cefpodoxime Proxetil in Bulk and Pharmaceutical Formulation by Using UV Spectrophotometer. American Journal of PharmTech Research 2014.

INTRODUCTION

Cefpodoxime proxetil is an oral broad spectrum prodrug of third generation cephalosporin. It is active against most gram positive and gram negative organisms responsible for various diseases such as respiratory tract infections, acuteotitis media, pharyngitis, sinusitis, uncomplicated gonorrhea and urinary tract infections.[1-2]. Literature survey revealed that few analytical methods are available for the individual estimation of cefpodoxime proxetil by HPTLC[4] and by HPLC[5-12] method in biological fluid and by UV spectrophotometric method[13-17]. But single estimation of this drug with 0.1N NaOH as solvent has not been reported in bulk and in pharmaceutical formulation.

Thus, the aim of the present work was to develop and validate a simple, reproducible and economic analytical method to estimate cefpodoxime proxetil in routine analysis.

MATERIALS AND METHOD

Materials:

Pure Standard of cefpodoxime proxetil powder was received as a kind gift from IBN SINA Pharmaceutical Industry Ltd., Bangladesh which was used as reference standard. The commercial cefpodoxime proxetil dosage forms used were tablet Dofixevi -200mg and suspension Metoxim **(40 mg/5mL)** were purchased from the local market.

Apparatus:

A Shimadzu UV-Visible spectrophotometer UV-1800 was used.

METHOD DEVELOPMENT

Preparation of stock standard

The standard stock solution of 100 µg/mL of cefpodoxime proxetil was prepared by weighing 100 mg of the drug, taken in 1000 mL volumetric flask and diluted with 0.1N NaOH.

Determination of wavelength of maximum absorption:

By appropriate dilution of standard stock solutions, different solutions containing different concentration (5, 10, 15, 20, &25µg/mL) of cefpodoxime proxetil were scanned in the range of 200-800 nm to determine the wavelength of maximum absorbance. Cefpodoxime proxetil has shown maximum absorption at 231 nm.

METHOD VALIDATION:

The proposed method was validated for different parameters like linearity, precision, accuracy, specificity, robustness, LOD, LOQ and assay.

Linearity Study:

The linearity was determined by plotting concentration against corresponding absorbance. Standard stock solutions, 100µg/mL were further diluted with solvent to obtain 5µg/mL-25µg/mL solutions. The calibration curves were constructed by plotting absorbance versus concentration and the regression equations were calculated.

Intra-day precision study:

Aliquots (0.5,1.5 and 2.5mL) of the 100µg/mL cefpodoxime proxetil stock solution were taken in three volumetric flask and respectively diluted with solvent to obtain three concentrations of 5, 15 and 25 µg/ml, respectively. Triplicate absorbance measurements of each were made in thrice time i.e. zero hour, fourth hour and eighth hour and the percentage RSD was calculated.

Inter-day precision study:

The selected concentrations for the intra-day precision study were again analysed for consecutive three days and the percentage RSD was calculated.

Accuracy and Recovery Studies:

Accuracy of the method was calculated by recovery studies at three different levels (75%, 100% and 125%) by standard addition method to study the accuracy of the method and to check the interference from excipients. The first recovery study was conducted on the excipients mixture (placebo) prepared by adding accurately weighed amounts of cefpodoxime proxetil to the excipient mixture and calculating the percentage recovery in each case.

Specificity in the presence of excipients:

The specificity test was carried out using only excipients. Spectra for placebo granules, blank and sample were measured and compared. The sample solution was kept in the oven (60^0C) and under the UV lamp (254 nm) for 72h in order to verify that none of the degradation products interfered with the quantification of the drug.

Robustness:

The robustness of an analytical procedure is the measure of its capacity to remain unaffected by small but deliberate variations in method parameters and provides an indication of its reliability during normal usage. It was determined by carrying out the analysis by two analysts at two different temperatures i.e. at 20^0C and 30^0C. The absorbance was measured and assay was calculated for six times.

Limit of Detection (LOD) and Limit of Quantitation (LOQ):

LOD and LOQ were calculated from the data obtained from the linearity studies. The slope of the linearity plot was determined. For each of the ten replicate determinations of same concentration (10µg/mL), standard deviation (SD) of the responses was calculated. Limit of

detection can be calculated by using the following formula:

LOD = 3.3 σ/ S

Limit of quantitation can be calculated base on standard deviation of the response and the slope.

LOQ = 10 σ/ S

Where σ = Standard deviation of the response; S = Slope of the calibration curve.

Assay of cefpodoxime proxetil formulations available in Bangladesh:

Twenty tablets were individually weighed and triturated to obtain homogeneous mixture. An amount of powder equivalent to 10mg of cefpodoxime proxetil was taken in 100mL volumetric flask and was diluted with 0.1N NaOH to make 100µg/mL and was sonicated for 20 min to effect complete dissolution of cefpodoxime proxetil, the solution was then filtered. The aliquot of the filtrate was further diluted to get final concentration of 10µg/mL of cefpodoxime proxetil. The % assay of the drug was calculated.

To analyze the concentration of cefpodoxime proxetil suspension, 1.5mL of cefpodoxime proxetil (which contain 8 mg mL^{-1}) was transferred in 100ml volumetric flask and was diluted with 0.1N NaOH. This solution was further diluted to get final concentration of 12µg/mL of cefpodoxime proxetil. The % assay of the drug was calculated. All determinations were conducted by thrice time.

Statistical analysis:

The results were expressed as mean±SD. Some results were expressed as %RSD.

RESULTS AND DISCUSSION:

The method discussed in the present work provides a convenient and accurate way for analysis of cefpodoxime proxetil. The different concentrations of 5-25 µg/mL were scanned and the wavelength of maximum absorption was found at 231 nm (Figure 1).

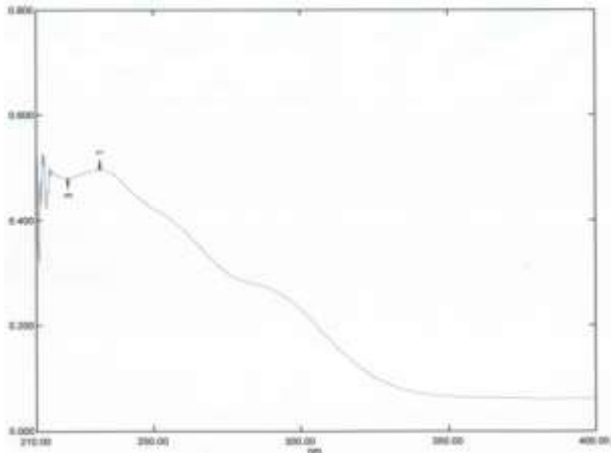

Figure 1: UV spectrum of cefpodoxime proxetil (λ_{max})

The drug obeyed the Beer's law with the concentration range 5– 25 µg/mL having line equation y = 0.0331x + 0.0151with correlation coefficient $R^2$of 0.998 and represented excellent linear relationship of the newly developed method (Figure 2).The LOD and LOQ of the developed method were determined by injecting progressively low concentrations of the standard solution (10 µg/mL) for 6 times and the values of LOD and LOQ were found to be 0.081µg/mL and 0.121µg/mL respectively.

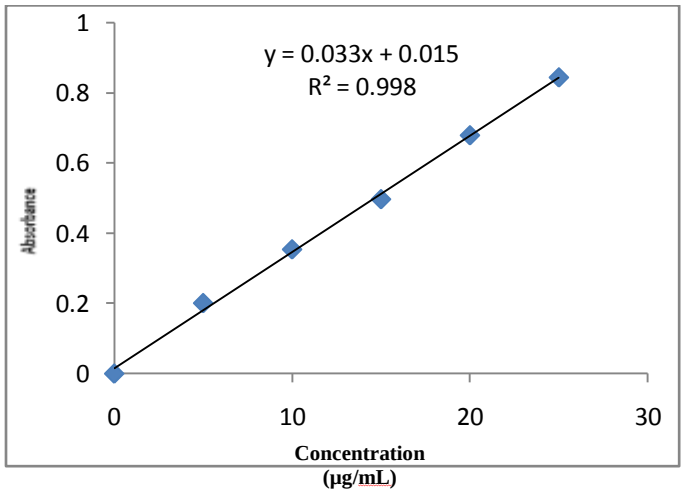

Figure 2. Calibration curve for cefpodoxime proxetil

The precision of the proposed method was checked by intra-day and inter-day repeatability of responses which confirmed adequate sample stability and method reliability over 24 h periods where RSD% amongst responses was found as < 2% (Table 1).

The accuracy was evaluated at three different concentrations which were conducted in successive analysis (n = 3) using the proposed method and the value was expressed as percentage of recovery between the mean concentrations of recovered and injected concentration of the drug. The average recoveries were found to be as 99.80%, 100.02% and 99.92% for the concentration levels of 75%, 100% and 125% respectively (Table 2).

The assays were validated by means of the analysis of variance. Cefpodoxime proxetil content in two pharmaceutical dosage forms (tablet and suspension) were determined by this proposed method which were in good agreement with the label claims with RSD value of 0.02% for tablet and 0.01% for suspension (Table 3).The %RSD was found in the range of 0.126 – 0.313% for robustness and ruggedness. The specificity of the analytical method was proved by comparing the spectra of placebo and degradation product of sample solution with that of accuracy sample.

All experimental results were within the range of the acceptability which indicated that the developed method was sensitive enough and accurate for quantitative analysis of cefpodoxime

proxetil. Therefore, the method was applied for quantitative analysis of cefpodoxime proxetil in bulk and pharmaceutical dosage form.

Table 1: Intra-day and inter-day precision determined for different concentrations of cefpodoxime proxetil

	Inter-day precision		Intra-day precision	
Concentration (µg/mL)	**Absorbance measured (Mean± SD)**	**% RSD**	**Absorbance measured (Mean± SD)**	**% RSD**
5	0.201 ± 0.0003	0.181	0.202 ± 0.0009	0.446
15	0.497 ± 0.0009	0.149	0.499 ± 0.0007	0.140
25	0.844 ± 0.001	0.118	0.863 ± 0.0012	0.139

Table 2.Determination of accuracy of cefpodoxime proxetil by UV-Visible spectrophotometer (n=3)

% Recovery	**Concentration(µg/mL)**		**% Avg. Recovery**	**% RSD**
	Amount added	**Amount found**		
75	5	4.99 ± 0.0055	99.80	0.006
100	15	15.03 ± 0.0077	100.02	0.008
125	25	24.98 ± 0.0091	99.92	0.009

Table 3: Assay of cefpodoxime proxetil in marketed products (n=3)

Pharmaceutical Dosage Form	**Declared concentration**	**Found concentration**	**Content (%)**	**% RSD**
Tablet (200 mg)	10	9.99 ± 0.02	99.90% ±0.02	0.02
Suspension (50mL) (8mg mL^{-1})	12	11.98 ± 0.01	99.83% ± 0.01	0.01

CONCLUSION:

This UV-spectrophotometric technique was quite simple, accurate, precise, reproducible and sensitive. The UV method has been developed for quantification of cefpodoxime proxetil in pharmaceutical dosage forms. The validation procedure confirms that this is a workable method for their quantification in the raw material and also in the formulations.

REFERENCES:

1. Lester AM. Antibiotics and antimicrobial agents. In: David AM, Thomas LL. Foye's Principle of Medicinal Chemistry. 5th ed, Davi T. Philadelphia: Lippncott Williams and Wilkins; 2002; 840-852.
2. Wesley MG, Todd UK. Cefpodoxime proxetil: A comprehensive review. Int J Antimicrob Agents.1994;4:37–62.
3. Sweetman S.C. In Martindale, The Complete Drug Reference. London: Pharmaceutical Press, London, 32nd ed., 1999;165-166, 233.

4. Darji BH, Shah NJ, Patel AT, Patel NM. Development and validation of a HPTLC method for the estimation of cefpodoxime proxetil. Indian J Pharm Sci [serial online] 2007;69:331–3.
5. Lee KY, Nurok D, Zlatkis A. Determination of cefpodoxime proxetil by High Performance Liquid Chromatography. J Chromatogr A 1997; 174: 187.
6. Kakumanu VK, Arora VK, Bansal AK. Development and validation of isomer specific RP-HPLC method for quantification of cefpodoxime proxetil extraction method coupled with HPLC-UV. J Chromatogr B 2006; 835: 16.
7. Naoto F, Yuichi S, Takao K, Koichi S, Hiroyuki N. LC/MS/MS method for the determination of trace amounts of cefmetazole and cefpodoxime proxetil contaminants in pharmaceutical manufacturing environments. J Pharm Biomed Anal 2006; 41: 1243.
8. Demetra K, Helen G, Zoe A, Nickolas V, Stavroula P, Thomas G, Garyphalia P, Agissilaos H, George K Cefpodoxime-Proxetil versus Trimethoprim-Sulfamethoxazole for Short Term Therapy of Uncomplicated Acute Cystitis in Women. Antimicrob Agents Chemother 2003; 47 **:** 897-900.
9. Aleksic M, Ilic M, Kapetanovic V. Adsorptive properties of cefpodoxime proxetil as a tool for a new method of its determination in urine. J Pharm Biomed Anal 2004; 36(4): 899-903.
10. Shah PB, Pundakrikakshudu K. RP-HPLC for the determination of cefpodoxime proxetil. Indian Drugs. 2006;43:126–8.
11. Kakumanu VK, Arora VK, Bansal AK. Development and validation of isomer specific RP HPLC method for quantification of cefpodoxime proxetil. J Chromatogra B. 2006;835:16–20.
12. Campus F, Deslandes A, Harcouet L, Farinotti R. High performance liquid chromatographic method for the determination of cefpodoxime level in plasma and sinus mucosa. J Chromatogr B Biomed Appl.1994;656:383–8.
13. Singh Sunil, Dubey Nitin, Jain Dinesh Kumar, Tyagi Lalit Kumar and Singh Mahendra. Spectrophotometric and RP-HPLC Methods for Simultaneous Determination of Cefpodoxime Proxetil and Clavulanate Potassium in Combined Tablet Dosage Form. American-Eurasian Journal of Scientific Research 5(2); 88-93, 2010.
14. Vilas D. Patil, R.Y.Chaudari, Spectrophotometric method for estimation of cefpodoxime proxetil and ofloxacin in tablet dosage form by simultaneous equation method. Int. J. Pharm. Life Sci.; 2012;3(9).
15. G.Abirami, T.Vetrichelvan, M.Bhavyasri. Development and Validation of UV Spectroscopy Method for the Determination of Cefpodoxime Proxetil and Ambroxol Hydrochloride in Pharmaceutical Formulation. Int J. PharmTech Res.2012,4(2)

16. Siddalinga Swamy MS, A Sathish Kumar Shetty, Anil kumar S.M. UV-Visible Spectrophotometric Methods For The Estimation Of Cefpodoxime Proxetil In Bulk Drug And Pharmaceutical Dosage Form. Int. J. PharmTech Res.2012,4(2)
17. Shah PB, Pundakrikakshudu K. Spectroscopic method for the determination of cefpodoxime proxetil. Indian Drugs. 2005;42:94–7.