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Development and Validation of Simultaneous Estimation of Cefpodoxime proxetil and Dicloxacillin sodium by Spectroscopic method in combined tablet dosage form

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Abstract: Simultaneous spectroscopic estimation of Cefpodoxime Proxetil and Dicloxacillin Sodium in their combine dosage form was developed and validated. The method was performed on Jasco V-530, model UV-2075 Spectrophotometer with Spectra manager as a software. Methanol was as a solvent for analysis. Detection was carried out at 234 nm for Cefpodoxime Proxetil and 276 nm for Dicloxacillin Sodium. Linearity was observed at concentration range 2.5-20 µg/ml for Cefpodoxime Proxetil and 12.5-100 µg/ml for Dicloxacillin Sodium. Correlation coefficient for Cefpodoxime Proxetil and Dicloxacillin Sodium was found 0.999 and 0.997 respectively. The method can successfully applicable to routine analysis.
Key words: Cefpodoxime Proxetil, Dicloxacillin Sodium, Methanol.

Introduction:

[1,2]Cefpodoxime Proxetil is Third Generation Cephalosporin Antibiotic and it is chemically (6R,7R)-7-[(2Z)-2-(2-amino-1,3-thiazol-4-yl)-2-(methoxyimino)acetamido]-3-(methoxymethyl)-8-oxo-5-thia-1-azabicyclo [4.2.0] oct-2-ene-2-carboxylic acid . Dicloxacillin Sodium is Anti-Bacterial -One of the penicillins which is resistant to penicillinase and chemically it is (2S,5R,6R)-6-[3-(2,6-dichlorophenyl)-5-methyl-1,2-oxazole-4-amido]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0] heptane-2-carboxylic acid. Structure of Cefpodoxime Proxetil is illustrated in fig.I. Structure of Dicloxacillin Sodium is illustrated in fig.II.

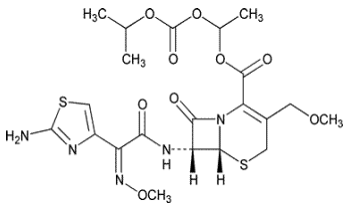

Figure I: Structure Of Cefpodoxime Proxetil

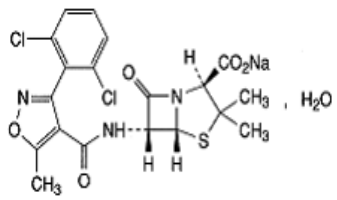

Figure II: Structure Of Dicloxacillin Sodium

So far, to our present knowledge, no single Simultaneous spectroscopic method for estimation of Cefpodoxime Proxetil and Dicloxacillin Sodium has been reported. [4-6]So an attempt was made to develop

single, accurate, rapid, and precise Spectroscopic method for the determination of Cefpodoxime Proxetil and Dicloxacillin Sodium.

Material and Methods:

Instruments:

Jasco V-530, model UV-2075 Double beam UV–visible spectrophotometer instrument was used in this method. Spectra Manager was used as a software for analysis.

Reagent and chemicals:

Cefpodoxime Proxetil and Dicloxacillin Sodium was a gift sample from Baroque pharmaceutical Limited, Khambhat. All chemicals and reagent used were analytical grade and purchased from Ranbaxy fine chemicals Limited. Combined tablet formulations (Zedocef-DXL-200) were procured from Indian market.

Preparation of standard stock solution:

Accurately weigh 50 mg of Cefpodoxime Proxetil and Dicloxacillin Sodium in 50ml volumetric flask and make up the volume with methanol which gives final strength about 1000µg/ml.

Selection of wavelength

Appropriate volume of Cefpodoxime Proxetil and Dicloxacillin Sodium about 1ml and 5ml were respectively taken in 50ml volumetric flask and volume was made up to mark with methanol. The resuitng solution was scanned in UV range (200 nm- 400nm). In the spectrum of Cefpodoxime Proxetil and Dicloxacillin Sodium 234 nm and 276 nm is selected respectively for simultaneous estimation.

Preparation of calibration curve:

To construct calibration curve Suitable amount of each solution was diluted with methanol in 50 ml volumetric flask as mentioned in table no I.

Table No I: Preparation of Calibration Curve

No	Cefpodoxime proxetil (ml)	Dicloxacillin Sodium(ml)	Composition µg/ml	
			Cefpodoxime proxetil	Dicloxacillin sodium
1	0.125	0.625	2.5	12.5
2	0.25	1.25	5	25
3	0.5	2.5	10	50
4	0.75	3.75	15	75
5	1	5	20	100

In the series, mixture of Cefpodoxime Proxetil and Dicloxacillin Sodium solutions having various concentrations of Cefpodoxime Proxetil (2.5-20 µg/ml) and Dicloxacillin Sodium (12.5-100 µg/ml) were prepared by mixing appropriate volumes of corresponding standard solution in a series of 50 ml volumetric flasks and diluted to volume with methanol.

Analysis of commercial formulation:

Twenty tablets were weighed and the average weight was calculated a quantity of mixed content of 20 tablets equivalent to 100mg and 500 mg of Cefpodoxime Proxetil and Dicloxacillin Sodium was accurately weighed and transferred in to 100 ml volumetric flask. The solution is dilute up to 100 ml with methanol.

Then 10 ml of above solution was diluted up to 100 ml with methanol which gives 100 µg/ml of Cefpodoxime Proxetil and 500 µg/ml Dicloxacillin Sodium. Than 10 ml of above solution was diluted up to 100

ml with methanol which gives 10 µg/ml of Cefpodoxime Proxetil and 50µg/ml Dicloxacillin Sodium in the formulation was determined by use of calibration curve.

Result and discussion:

The method was validated by establishing linearity, accuracy, interday and intraday precision of measurement of sample application. The limit of detection and limit of quantification were also determined.

Linearity calibration curve:

The stock solutions were diluted in concentration range of 2.5-20 µg/ml for Cefpodoxime Proxetil and 12.5-100 µg/ml Dicloxacillin Sodium and data was evaluated by regression analysis. Five concentration points were assayed in triplicate. Both Cefpodoxime Proxetil and Dicloxacillin Sodium showed good linearity in tested range. The regression coefficient (R2) Value for Cefpodoxime Proxetil and Dicloxacillin Sodium were found to be 0.999 and 0.997 respectively. Overlay Linearity curve for Cefpodoxime Proxetil and Dicloxacillin Sodium was shown in figure no III. Calibration curve for Cefpodoxime Proxetil and Dicloxacillin Sodium was shown in figure no IV and V respectively.

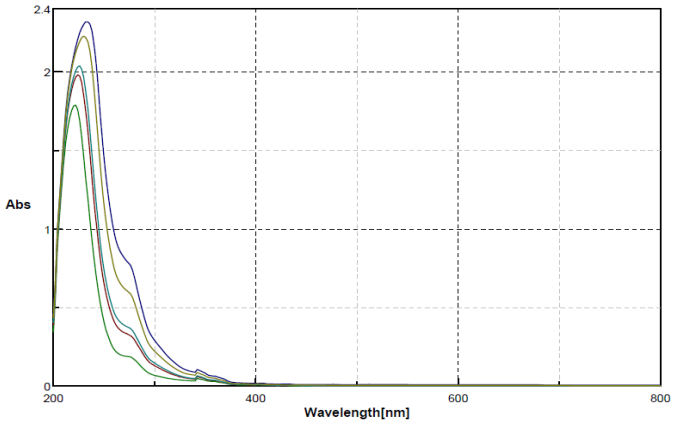

Figure no III: Linearity Of Dicloxacillin Sodium And Cefpodoxime Proxetil.

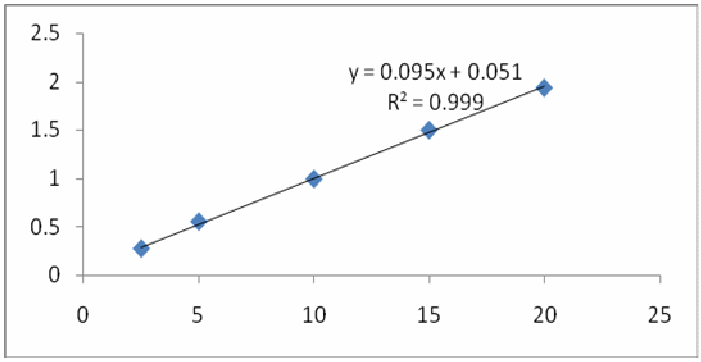

Figure no IV: calibration curve of cefpodoxime proxetil.

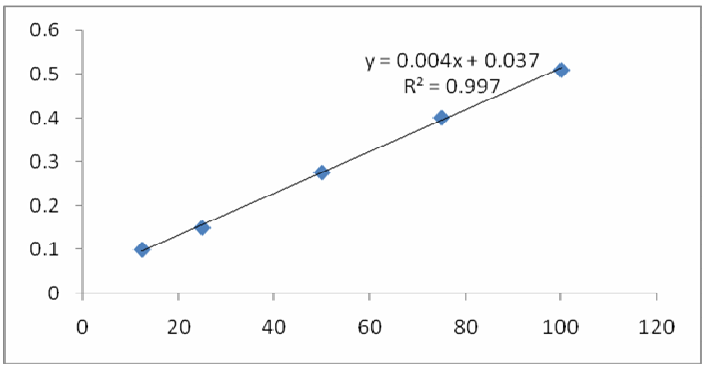

Figure no V: calibration curve of Dicloxacilin sodium.

Accuracy:[09]

Recovery study was carried out for accuracy parameter. The study was carried out at three level. To powder formulation the standard drug Cefpodoxime Proxetil and Dicloxacillin Sodium were added 80%, 100%, 120% levels, dilution were made and analyzed by the method. The % recovery were calculated and found to be within the limit. Result for accuracy study is shown in table no II.

Table No II: Results For Recovery Study

Level	Spike (mcg/ml)		Absorbance of Spike		Found Concentration		%Recovery	
	Cefpo	Diclo	At 234 nm	At 276 nm	Cefpo	Diclo	Cefpo	Diclo
80%	8.00	40.00	0.811	0.199	8.00	40.50	100.00	101.25
	8.00	40.00	0.801	0.198	7.89	40.25	98.68	100.63
	8.00	40.00	0.800	0.197	7.88	40.00	98.55	100.00
100%	10.00	50.00	0.998	0.275	10.20	50.53	102.00	101.06
	10.00	50.00	0.994	0.266	10.17	51.00	101.70	102.00
	10.00	50.00	0.999	0.272	10.00	51.00	100.00	102.00
120%	12.00	60.00	1.200	0.322	12.00	61.00	100.00	101.67
	12.00	60.00	1.192	0.322	12.00	61.00	100.00	101.67
	12.00	60.00	1.194	0.276	12.20	60.92	101.67	101.53
Average							100.13	101.23

Precision: [09]

Intraday precision was found by analysis of standard drug at six times on the same day, While interday assay precision was carried out on six different day. The RSD was found to be less than 2 for both interday precision and intraday precision. Result for the interday precision and intraday precision is shown in table no III, IV respectively.

Table No III: Results of Interday Precision

Concentration		Absorption		Found Concentration		% Assay	
Cefpo	Diclo	Cefpo	Diclo	Cefpo	Diclo	Cefpo	Diclo
100%	100%	0.994	0.267	10.20	51.00	102.0	102.0
100%	100%	0.994	0.266	10.10	51.00	101.0	102.0
100%	100%	0.990	0.266	10.19	51.00	101.9	102.0
100%	100%	0.990	0.265	10.13	51.00	101.3	102.0
100%	100%	0.980	0.270	10.17	49.62	101.7	99.2
100%	100%	0.979	0.267	10.20	49.96	102.0	99.9
Average						101.7	101.2
SD						0.4	1.3
%RSD						0.41	1.25

Table No IV: Results of Intraday Precision

Concentration		Absorption		Found Concentration		% Assay	
Cefpo	**Diclo**	**Cefpo**	**Diclo**	**Cefpo**	**Diclo**	**Cefpo**	**Diclo**
100%	100%	0.979	0.268	10.20	49.82	102.0	99.6
100%	100%	0.978	0.265	10.20	50.15	102.0	100.3
100%	100%	0.978	0.264	10.14	50.29	101.4	100.6
100%	100%	0.978	0.265	10.20	50.15	102.0	100.3
100%	100%	0.980	0.270	10.17	49.62	101.7	99.2
100%	100%	0.979	0.265	10.19	50.24	101.9	100.5
Average						101.8	100.1
SD						0.2	0.5
%RSD						0.24	0.53

Conclusion:

A relatively simple simultaneous equation method was optimized and validated with system suitability for the simultaneous determination of the Cefpodoxime Proxetil and Dicloxacillin Sodium. The method validation according to the ICH guidelines. The validation data indicate good precision, accuracy and reliability of the method. The developed method offers several advantages in terms of simplicity in mobile phase, retention time, easy sample preparation steps and comparative short run time which makes the method specific and reliable for its intended use in simultaneous determination of Cefpodoxime Proxetil and Dicloxacillin Sodium in tablet dosage forms. Summary of validation parameters is shown in table no IV.

Table No V: Summary of Validation Parameters

Sr No	Validation parameter	Specific Characteristics	Cefpodoxime Proxetil	Diclocxacillin Sodium
1	Linearity	Range Correlation coefficient	2.5-20 µg/ml 0.999	12.5-100 µg/ml 0.997
2	Sensitivity	Limit of quantification	0.06 %RSD	0.02 %RSD
		Limit of detection	0.03 %RSD	0.01 %RSD
3	Precision (%RSD)	Method precision Interday precision Intraday Precision	 0.41 0.24	 1.25 0.53
4	Accuracy	% recovery	100.13	101.23
5	Assay	% amount of drug found in tablet	99.23%	100.01%

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