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Simultaneous Estimation of Cefoperazone and Sulbactam in Bulk and Multicomponent Formulation

ASHA THOMAS*, S.A. KANDGAONKAR, LATA KOTHAPALLI, SUMITRA JANGAM, S. BODKHE, MANISHA PATANKAR and A.D.DESHPANDE
Department of Pharmaceutical Chemistry, Padmashri Dr. D.Y. Patil Institute of Pharmaceutical Sciences and Research, Pimpri, Pune-411 018, India
E-mail: dypharma@yahoo.co.in

A novel, simple, sensitive, rapid, accurate and economical spectrophotometric method has been developed for the simultaneous estimation of cefoperazone sodium and sulbactam sodium in bulk and combined dosage form. This method involves solving of simultaneous equations based on measurement of AUC at two wavelengths ranges 259-269 and 220-228 nm. Both the drugs obeyed the Beer's law in the concentration ranges employed for this method. The results of the analysis were validated statistically and by recovery studies.

Key Words: Cefoperazone, Sulbactam, Estimation.

INTRODUCTION

Cefoperazone sodium (CPZ), chemically 5-thia-1-azabicyclo[4.2.0]oct-ene-2-carboxylic acid, 7-[[[[(4-ethyl-2,3-dioxo-1-piperazinyl)carbonyl]-amino](4-hydroxyphenyl)acetyl]amino]-3-[[(1-methyl-1H-tetrazol-5-yl)thio]methyl]-8-oxo-, monosodium salt is a broad spectrum cephalosporin antibiotic[1,2]. Cefoperazone is a third generation cephalosporin, which acts against sensitive organisms during the stage of active multiplication by inhibiting biosynthesis of cell wall mucopeptide. Cefoperazone is active against a wide range of gram-positive and gram-negative bacteria, including *Enterobacteriaceae* and *Pseudomonas* species[3].

Sulbactam sodium (SBT), chemically 4-thia-1-azabicyclo[3.2.0]-heptane-2-carboxylic acid-3,3-dimethyl-7-oxo-4,4-dioxide, sodium salt, is an irreversible β-lactamase inhibitor[1,2]. Sulbactam have low antibacterial activity but are able to inhibit β-lactamases that destroy β-lactam antibiotics like penicillins and cephalosporins. It is an irreversible inhibitor of many plasmid-mediated and some chromosomal β-lactamases and has similar spectrum of β-lactamase inhibition to clavulanic acid. Sulbactam increases the antibacterial spectrum and clinical effectiveness of cefoperazone against pathogens such as plasmid containing enteric bacilli, Bacteroids species and Acinetobacter species and possibly provide opportunity to reduce dosage schedules for infecting species already susceptible to cefoperazone alone[3].

Literature survey reveals that few UV[4,5], HPLC[6-11] and colorimetric[12,13] methods have been reported for determination of both the drugs as single components in bulk, formulations and in biological fluids. Combination of 500 mg of cefoperazone sodium and 500 mg of sulbactam sodium are now becoming available to the market by some companies. The objective of the investigation was to develop and validate a UV spectrophotometric method for the simultaneous estimation of the combined dosage form.

EXPERIMENTAL

A Shimadzu UV/Visible spectrophotometer model 1700 (Japan) was employed with spectral bandwidth of 2 nm and wavelength accuracy of ± 0.5 nm, with automatic wavelength correction, with a pair of 10 mm quartz cells. A Shimadzu electronic analytical balance (AX-200) was used for weighing the sample. Cefoperazone sodium (Hindustan Antibiotics) and Sulbactam sodium (Aurbindo Pharmaceuticals) and NaOH AR grade (Qualigens Fine Chemicals, Mumbai)) were used in the study.

Method simultaneous equation using area under the curve method

Standard stock solutions (100 µg/mL) of CPZ and SBT were prepared by dissolving separatively 10 mg of drug in 0.1 M NaOH. For the simultaneous determination using the area under the curve method, the solutions of the drugs were scanned in the range of 190-400 nm. The wavelength range selected for the analysis of cefoperazone sodium was between 220-228 nm at which cefoperazone sodium contributes to a larger AUC as compared to sulbactam sodium. For sulbactam sodium, the wavelength range selected was between 259-269 nm under which sulbactam sodium contributes to a larger AUC as compared to Cefoperazone sodium. The overlain spectras of CPZ and SBT along with its AUC are shown in Fig. 1. CPZ and SBT exhibited linearity with AUC in the concentration range of 10-50 µg/mL each at their respective selected wavelength ranges. Coefficient of correlation was found to be 0.9994 and 0.9995 for CPZ and SBT, respectively. The optical characteristics and validation data of the proposed methods are presented in Table-1.

For the simultaneous estimation of CPZ and SBT, mixed standard solutions of CPZ and SBT of concentrations within the Beer Lambert's range were prepared by appropriate dilution of standard stock solutions. The AUC of the mixed standard solutions were recorded at selected wavelength ranges. For the analysis of formulation *i.e.* dry powder for I.V. use, accurately *ca.* 10 mg powder sample was weighed, transferred to a 50 mL volumetric flask and dissolved in *ca.* 25 mL of 0.1 M NaOH. After immediate dissolution, the volume was made up to the mark with 0.1 M NaOH. The solution was diluted further to prepare sample solutions containing CPZ and SBT within its Beers-Lambert's ranges.The concentration of CPZ and SBT in the pure mixed standards and sample solutions were found by using eqn. 1 and 2.

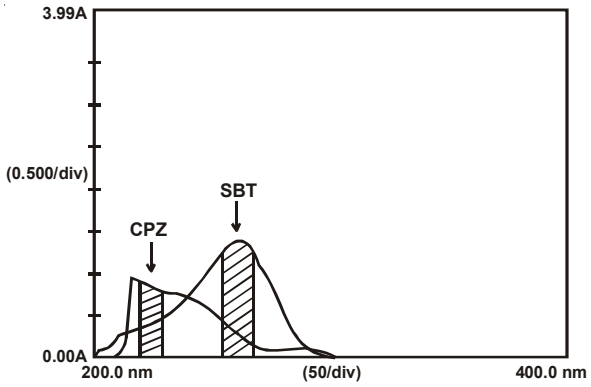

Fig. 1. Overlain spectra of CPZ and SBT showing AUC

TABLE-1
OPTICAL CHARACTERISTICS AND VALIDATION DATA OF CEFOPERAZONE SODIUM AND SULBACTAM SODIUM

Parameters		CPZ	SBT
Working λ (0.1 M NaOH) (nm)		220-228	259-269
Beer's Law range (μg/mL)		10-50	10-50
Molar absorptivity (L mol^{-1} cm^{-1})		18.44×10^4	30.18×10^4
Precision:*	Intraday	0.1473	0.1400
	Interday	0.2691	0.2308
LOD (μg/mL)*		0.00239	0.00382
LOQ (μg/mL)*		0.00796	0.0130
Regression values:	Slope*	0.2839	0.1194
	Y-Intercept*	-0.1005	-0.0236
	Regression Coefficient (r^2)*	0.9994	0.9995

*Average of six determinations.

$$C_{CPZ} = \frac{X_{S259-269} \times AUC^{M}_{220-228} - X_{S259-269} \times AUC^{M}_{259-269}}{X_{S259-269} \times D_{C220-228} - X_{S259-269} \times X_{S259-269}} \quad (1)$$

$$C_{SBT} = \frac{X_{C220-228} \times AUC^{M}_{259-269} - X_{C259-269} \times AUC^{M}_{220-228}}{X_{S259-269} \times X_{C220-228} - X_{C220-228} \times X_{C259-269}} \quad (2)$$

where C_{CPZ} = Concentration of Cefoperazone sodium, C_{SBT} = Concentration of Sulbactam sodium, $AUC^{M}_{259-269}$ = Area under curve of mixture at wavelength range 259-269 nm, $AUC^{M}_{220-228}$ = Area under curve of mixture at wavelength range 220-228 nm,

$$X_{S259-269} = \frac{\text{AUC of SBT at wavelength range } 259-269 \text{ nm}}{\text{Concentration of SBT in g/L}}$$

$$X_{S220-228} = \frac{\text{AUC of SBT at wavelength range } 220-228 \text{ nm}}{\text{Concentration of SBT in g/L}}$$

$$X_{C259-269} = \frac{\text{AUC of CPZ at wavelength range } 259-269 \text{ nm}}{\text{Concentration of CPZ in g/L}}$$

$$X_{C220-228} = \frac{\text{AUC of CPZ at wavelength range } 220-228 \text{ nm}}{\text{Concentration of CPZ in g/L}}$$

RESULTS AND DISCUSSION

The proposed method was validated by studying several parameters such as accuracy, precision, linearity, limit of detection (LOD) and limit of quantitation (LOQ). The accuracy of the proposed method was determined by performing recovery studies of CPZ and SBT at 80, 100 and 120 % of the test concentration as per ICH guidelines. The results of the formulation analysis, recovery studies and its statistical validation data given in Tables 2 and 3. The % recovery of the method was greater than 98 % and RSD did not exceed 2 % indicating high degree of accuracy and precision of the proposed method.

TABLE-2
STATISTICAL VALIDATION DATA OF FORMULATION ANALYSIS

Name of component	Amount present	Amount found* (%)	Standard deviation*	Co-efficient of variation*	Standard error*
CPZ	500	100.87	0.3636	0.3610	0.1484
SBT	500	100.59	0.4695	0.4671	0.1917

*Average of six determinations.

TABLE-3
RECOVERY STUDIES AND ITS STATISTICAL VALIDATION DATA

Level of recovery	Name of drug	Amount present (mg)	Amount of standard added (mg)	% Recovery* ± SD*	Coefficient of variation*	Standard error*
80	CPZ	500	400	100.06 ± 0.8549	0.8543	0.4936
	SBT	500	400	99.25 ± 0.3041	0.3064	0.1756
100	CPZ	500	500	100.65 ± 0.7858	0.7807	0.4537
	SBT	500	500	99.58 ± 0.9570	0.9610	0.5525
120	CPZ	500	600	99.96 ± 0.9573	0.9376	0.6888
	SBT	500	600	99.11 ± 0.7263	0.7328	0.4193

*Average of three determinations at each level of recovery

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