



## Fading Spectrophotometric Determination of Cefoperazone Sodium in Injections by Fe<sup>3+</sup>-Sulfosalicylic Acid System

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A new fading spectrophotometric methods was founded for the determination of cefoperazone sodium. In the acid medium, sulfosalicylic acid could react with Fe<sup>3+</sup> to form a complex which has the maximum absorbance at 510 nm. Fe(III) could be reduced to Fe(II) by sulfydryl which is the degradation product of cefoperazone sodium under heat condition. So the absorbance of binary complex Fe(III)-sulfosalicylic acid in the solution could be decreased by a decrease in the concentration of Fe(III) for the redox reaction between Fe(III) with sulfydryl. It was found that the concentration of cefoperazone sodium has a good linear with the absorbance. The parameter of the experiment was investigated and optimized. Under the optimum conditions, the absorbance and the concentration of ceftriaxone sodium was linear in the range of 0.50-12.5 mg/L. The regression equation was  $A = 0.04808c \text{ (mg/L)} + 0.523$ , the average recovery rate of samples in the system was 98.8-101.4 %. The proposed methods have been applied to the determination of cefoperazone sodium content in injections with satisfactory results.

**Key Words:** Spectrophotometry, Sulfosalicylic acid, Cefoperazone sodium.

### INTRODUCTION

Cefoperazone sodium is one of the third-generation semi-synthetic cephalosporins antibiotic active against a wide range of gram-positive and gram-negative bacteria and primarily used in clinical treatment of various sensitive bacteria infection<sup>1</sup>. Several analytical techniques have been used for quantification of cefoperazone sodium in pharmaceutical formulations and human biological fluids. These included spectrophotometry<sup>2-6</sup>, spectrofluorimetry<sup>7,8</sup>, colorimetry<sup>9</sup>, capillary zone electrophoresis<sup>10</sup>, voltammetry<sup>11,12</sup> and high-performance liquid chromatography<sup>13-18</sup>. In this work, a new spectrophotometric procedure for the determination of cefoperazone based on the formation of binary complex Fe(III)-sulfosalicylic acid. When heated in the weak acid medium, cefoperazone sodium could be degraded to form a new compound containing sulfydryl and Fe(III) could be reduced by the sulfydryl to form Fe(II) ion. So the absorbance of binary complex Fe(III)-sulfosalicylic acid in the solution could be decreased by a decrease in the concentration of Fe(III) for the redox reaction between Fe(III) with sulfydryl. It was found that the concentration of cefoperazone sodium has a good linear with the absorbance decreased. As the determination was carried out directly in injection sample, the method has advantages such as simplicity and low interference and has been successfully applied to determine in the injection of cefoperazon with satisfactory results.

### EXPERIMENTAL

UV-2550 spectrophotometer (Shimadzu Japan), A Model pHS-3C pH meter (Shanghai Rex Instrument Factory). All the reagents used were of analytical reagent grade and the solutions were prepared with distilled water unless otherwise specified.

A stock standard solution of cefoperazone (the National Institute for the Control of Pharmaceutical and Biological Products, the quality percentage is 99.8 %) at a concentration of 250 mg/mL was used. Working standard solutions were obtained by appropriate dilution of the stock standard solution. 500 mg/L Fe<sup>3+</sup> solution: 500 mg/L; sulfosalicylic acid solution (SSA): 12.5 g/L; Clark-Lubs buffer solutions over the pH range of 4.0-9.0 were prepared according to Ref<sup>19</sup>. In this case 0.2 mol/L KCl solution, 0.2 mol/L HCl and 0.2 mol/L potassium acid phthalate were the buffer components.

**Procedure:** Accurately remove appropriate amount cefoperazone sodium standard solution or sample solution to a 10 mL colorimetric tube equipped with plug. Followed by adding 1.50 mL, 500 mg/L ferric solution, then this solution in the colour comparison tube was put into the boiling water bath for 70 min after thorough mixing. After removing from the electric-heated thermostatic water bath, the solution was immediately cooled with current water, then treated with 1.50 mL, 12.50 g/L sulfosalicylic acid solution, 2 mL pH 5.0 C-L buffer solution, then completed to volume with distilled

water, mixed well and stood for 5 min. The absorbance was measured at 500 nm against a reagent blank in a 1 cm quartz cell.

## RESULTS AND DISCUSSION

**Absorption spectra:** The absorption spectra of cefoperazone-Fe(III)-sulfosalicylic acid and Fe<sup>3+</sup>-sulfosalicylic acid were scanned against the reagent blank, respectively in the wavelength range 480-560 nm (Fig. 1). It is clear that the wavelength at 500 nm was not changed but the absorbance was decreased by a decrease in the concentration of Fe(III). So 500 nm was selected for further study.

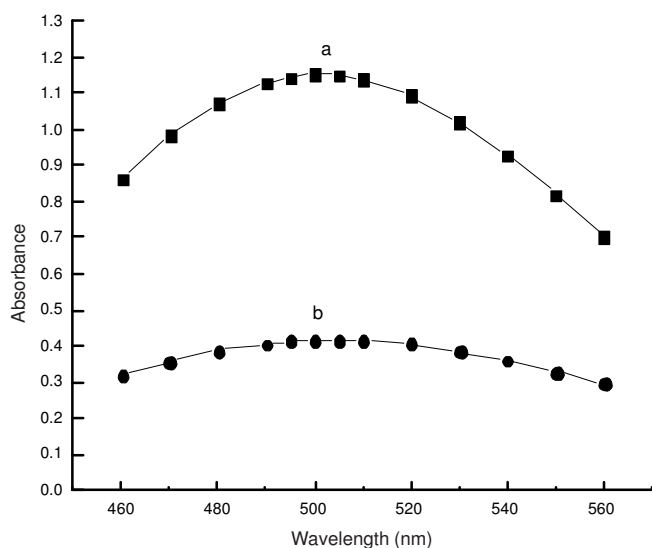


Fig. 1. Absorption spectra. (a) Fe<sup>3+</sup>-sulfosalicylic acid; (b) Cefoperazone-Fe<sup>3+</sup>-sulfosalicylic acid

**Effect of pH:** For the reaction between Fe(III) and sulfosalicylic acid was influenced significantly by the original concentration of H<sup>+</sup>, the effect of pH on the absorbance was examined over the range from pH 4-9. Clark-Lubs buffer solution was chosen to study the effect of reaction medium. The result was shown in Table-1. The absorbance showed a maximum and stable value at pH 5-8. The influence of different amounts of Clark-Lubs buffer solution (pH 5) on the system was also studied. The amount of Clark-Lubs solution has no effect on the absorbance. Thus, pH 5 as one of the test conditions was selected and the amount of buffer solution was chosen to 2 mL.

TABLE-1  
EFFECT OF pH

pH	4	5	6	7	8	9
A	0.498	0.526	0.521	0.530	0.519	0.478

**Effect of reaction temperature:** For oxidation-reduction reaction between cefoperazone sodium and Fe<sup>3+</sup> was not reacted at a lower temperature, a higher temperature could make this reaction proceeded fast. With the increased temperature, the speed of the reaction was increases. Therefore it must consider the effect of the reaction temperature. The result was shown in Table-2. It could be seen that the absorbance

increased with the rising of temperature. In order to facilitate control and make the reaction speed, 100 °C was selected.

TABLE-2  
EFFECT OF TEMPERATURE

Temp. (°C)	25	40	50	60	70	80	90	100
A	0.047	0.084	0.088	0.090	0.164	0.309	0.354	0.519

**Effect of the amounts of sulfosalicylic acid:** In this studied system, the sulfosalicylic acid was used as colour reagent and chelating agent and it was added excessive. The effect of the amount of added sulfosalicylic acid in the systems has been investigated on the absorbance and the result was illustrated in Fig. 2. As indicated in this figure, when the amount of sulfosalicylic acid was in the range of 0.50-3.00 mL, the absorbance was maximum and unchangeable. So in this work, 1.50 mL, 12.5 g/L sulfosalicylic acid solution was adopted for further study.

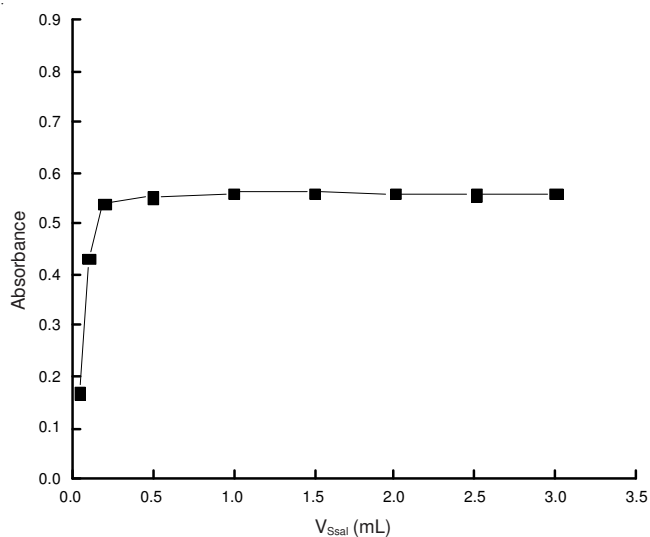


Fig. 2. Effect of sulfosalicylic acid

**Effect of the amount of Fe<sup>3+</sup>:** In order to made the reaction between the degradation product of cefoperazone sodium and Fe(III) reacted completely, the effect of the amount of Fe(III) on the absorbance was studied. The result was shown in Fig. 3. With the increased amount of Fe(III), the absorbance was increased correspondingly. When the amount of Fe(III) was in the range of 0.50-2.00 mL, it could be seen that the absorbance was maximum and stable. So the amount of 500 mg/L Fe<sup>3+</sup> was fixed at 1.50 mL.

**Effect of time of redox reaction and coordination reaction:** Though the reaction of trivalent iron and cefoperazone was accelerated in the boiling water, it still required a certain reaction time to complete. Meanwhile the stability of the complex formed from trivalent iron and sulfosalicylic acid must also be considered. Experiment investigated the influence of the redox reaction time and coordination stable time on absorbance. The experimental results showed that: with the increasing of reaction time, the absorbance increases gradually. After reacting at 100 °C for 70 min, the absorbance of the system got the maximum value and kept to be stable. It illustrated that the redox reaction reacted completely. After cooling

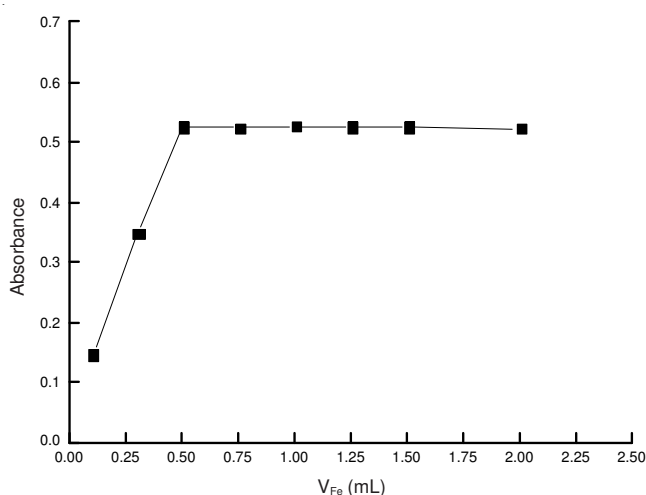


Fig. 3. Effect of Fe(III)

by water, the absorbance of the complex was stable after 5 min, the time of redox reduction reaction and coordination was choose as 70 and 5 min, respectively.

**Effect of coexisting substances:** The effect of various substances on the determination of 50 mg/L cefoperazone sodium was examined using the recommended procedure. A maximum error of  $\pm 5\%$  in the absorbance reading was considered tolerable. The common medic vehicle and the additive, such as lactose, glucose, starch, paste Jing, *etc.* were tested for coexisting substances. When the quantity added of the above material was equal to 500 times of cefoperazone sodium, the absorbance value is almost constant. That is to say these materials were not influence the measurement of cefoperzone sodium. Therefore after filtering, the sample could be measured directly without other pretreatment.

**Characteristics of the method:** Accurately put different volume of 50 mg/L cefoperazone sodium solution in test tube and followed by adding 1.50 mL of 500 mg/L  $\text{Fe}^{3+}$  solution, 1.5 mL of 12.5 g/L sulfosalicylic acid solution, 2 mL pH 5 the C-L buffer solution, the reagent blank was used as reference. Under the optimum conditions, the calibration graph was linear in the concentration range of 0.50-12.50 mg/L. The calibration equation is  $A = 0.04808c \text{ (mg/L)} + 0.5231 \text{ (c: mg L}^{-1}\text{)}$  with a correlation coefficient of 0.9990. The apparent molar absorption coefficients determined for the cefoperazone- $\text{Fe}^{3+}$ -sulfosalicylic acid associates was  $3.21 \times 10^4 \text{ L mol}^{-1} \text{ cm}^{-1}$ . The limit of detection (DL), defined as  $\text{DL} = 3\text{SB}/m$ , was 0.09 mg/L.

**Sample analysis and recovery experiment:** Accurately weigh a certain amount cefoperazone sodium powders obtained from the local market and completely dissolved into a 100 mL volumetric flask, then settled to the volume of 100 mL with distilled water. Put appropriate amount of the sample solution into a 10 mL colorimetric tube, then the following steps was followed as mentioned above and the experimental procedure was followed to complete the determination. The analytical results of in terms of cefoperazone sodium are shown in Table-3. The examination recovery was carrying out by adding certain amounts of standard solution to this sample

TABLE-3  
RESULT OF THE SAMPLE (n = 6)

Product batch	HPLC method (%)	Proposed method (%)	RSD (%)	Added (mg)	Found (mg)	Recovery (%)
110323	99.67	99.17	0.19	5.00	4.96	99.2
				8.00	7.91	98.9
110409	99.31	98.80	0.28	5.00	5.07	101.4
				8.00	8.03	100.4
110515	99.50	99.36	0.27	5.00	4.94	98.8
				8.00	8.08	101.0

solution and then the mixed solutions were measured by the recommended procedure. Different batches of sample content were listed, respectively. The relative standard deviation is less than  $\pm 1\%$ , the average recoveries was around 99.9 %.

### Conclusion

A simple and rapid method for the determination of cefoperazone in the injection samples has been proposed. The method does not require a pre-treatment process. The method has the advantage of being simple, reproducible, selective and sensitive. It is well suited for the determination of trace cefoperazone in the injection samples with satisfactory result.

### ACKNOWLEDGEMENTS

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