

Ceftazidime with other Drugs Complexation Studied by UV Spectrophotometrically and Exploration of Antimicrobial Activity, *In-Vitro* Investigation

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ABSTRACT

The Ceftazidime is an antibiotic of third-Generation of Cephalosporin. The cephalosporins have appeared as one of most widely ordered classes of the antibiotics in United States. The tremendous escalation of group of drug has been accompanied by the great perplexity as to their suitable use. Improper exercise of the cephalosporins has consequence in the bacterial resistance, excessive costs and clinical failures. The ceftazidime has been also used successfully in the Lower Respiratory Tract Infections, Skin and Skin-Structure Infections, Urinary Tract Infections, Bone and also Joint Infections, Central Nervous System Infections and also Intra-abdominal Infections. Ceftazidime has been interacted with Zn, Mg as the *in-vitro* examination. More to the point, the anti-microbial analysis of drugs along with complexes was determined. It has also scrutinized that the Ceftazidime interrelates with the metal and also antacid on pH 7.4 by the plotting a variety of UV Spectrophotometric methods. This examine also authenticates that there was a interaction between Ceftazidime with metal and also antacid which was the authenticated by the job's plot technique additionally by the antimicrobial exploration. This was also authenticated that the region of the inhibition of Ceftazidime with Metal as well as antacid squeezed from 16 mm to 14 mm and 15 mm correspondingly. The typical Ceftazidime disk checked against *Staphylococcus aureus*.

Introduction

Ceftazidime is the semisynthetic, beta-lactam, broad-spectrum, antibacterial drug for the parenteral administration. This is a pentahydrate of pyridinium compound [1]. At this time drug interaction be competent of the simply be dissimilar as the interaction connecting a drug in addition to additional material with intention of the stop medicine commencing the phase as expected [2]. These correlations may happen by reason of be short of the knowledge regarding the principle ingredients associated in related substances [3]. Two medicines are antagonistic at what time their interaction occurs a reduce in special effects of one or else both of medicines. The dissimilar responses of receptor to act of a medicine has effected in number of arrangements, which use expressions such as "partial agonist", "competitive agonist" etc. This is even expected that a lot of authors would mismanage any given

arrangement [4] Commonly iron complexes were used in convey of oxygen in human blood as well as tissues. An mature at rest takes 250ml of uncontaminated oxygen for each minute, these oxygen conceded by metal complex convey system recognized heame, alloying oxygen to go away the blood at what time it arrives the tissue [5]. Antibiotic and metal interaction and successfully found there after interaction result. Also, the antimicrobial activity of drug and the metals complexes were determined. This has been seen that the antibiotic interacts along with metal at the pH 7.4. The different essential metal intricate of the many drugs has been synthesized in addition to characterized by the techniques like NMR, UV, atomic absorption, FT-IR as well as elemental analysis. Spectroscopic, IR Spectroscopic, disk diffusion method, Biological assay studies of complexes [6]. On the other hand in this interaction there uses metals complex which are interaction with drug into our

body. And have been use there various type of bacteria for finding zone of inhibition. Some paper there uses methanol and ethanol for disk diffusion result clearly showing [7].

Materials & Methods

(Tables 1 & 2) Ceftazidime stock solutions 250 milliliter of the 1×10^{-2} Molar was set by the softening 1.386 gm of Ceftazidime solution in 250 milliliters of Demineralized Water (DMW) in a 250 milliliters volumetric flask. The reserve solutions were thinned to the desired potency by buffer solutions [8].

Table 1: List of chemicals and reagents.

Serial No	Name	Source
1	Ceftazidime	Gift samples from Incepta pharmaceuticals Ltd.
2	Zinc Sulphate (Metal)	Merck ltd, Mumbai, India
3	Magnesium Hydroxide (Antacid)	Merck ltd, Mumbai, India
4	Sodium di-hydrogen phosphate	USTC, Foys lake, Chittagong, dept of pharmacy
5	Disodium hydrogen phosphate	USTC, Foys lake, Chittagong, dept of pharmacy
6	Phosphate Buffer	USTC, Foys lake, Chittagong, dept of pharmacy

Table 2: List of instruments & equipments.

Name	Model	Source
pH Meter	PH-211	Hanna,Romania
UV Spectrophotometer	T80	PG instrument Ltd, England
Electronic Balance	AL-204	Mettlertoledo, Switzerland
Pipette		Fischer scientific,Germany

Preparation of Metal Solutions

For the basis of 0.01 Molar Zn solution such as zinc sulfate hepta hydrate (precisely 0.28754 gm) was assessed exactly in addition to the initiated with assist of funnel in the 100 ml volumetric flasks, softened in the DM water in addition to the framework to mark by the alike solvent. These principal solutions were supplementary diluted ten folds in equivalent solvent in company with the concluding solution was 0.0001 M concentration.

Preparation of Antacid Solutions

For the grounding of 0.01 Molar antacid solution like $Mg(OH)_2$ (0.0740gm) was assessed accurately as well as initiated with facilitate of the funnel in the 100 milliliters volumetric flask, and softened in demineralized water also construct up to the mark by identical solvent. This primary solution was further diluted ten crinkles in the identical solvents and the final also solutions were 0.0001 M concentrations.

Grounding of the Buffer Solutions

To get set buffer solution 1.76 grams of disodium hydrogen phosphate was softened in demineralized water by 2.43 grams of

solution dihydrogen phosphate in addition to the pH was adjusted to pH 7.4 as well as volume was also completed to 1000 milliliters with equivalent solution.

Grounding of the Typical Curve of the Ceftazidime

Ceftazidime reserve solutions at pH 7.4 in addition to the concentrations of 1×10^{-5} Molar was introduced in unlike concentration to 10 test tubes and to have later concentrations resembling 9×10^{-5} Molar, 8×10^{-5} Molar, 7×10^{-5} Molar, 6×10^{-5} Molar, 5×10^{-5} Molar, 4×10^{-5} Molar, 3×10^{-5} Molar, 2×10^{-5} Molar, 1×10^{-5} Molar. Now solutions were rightfully mixed. Then absorbance rates of solutions were found at the 500 nm throughout UV spectrometer [9].

Using Disc Diffusion Process

Solution of commemorated concentrations (Like $3 \mu\text{g/ml}$) of test samples were completed during dissolving measured quantity of trials in calculated quantity of solvents. The dried in addition to sterilized filter paper discs (such as 6 mm as a diameter) are afterward impregnated with recognized amounts of trial matters by using micropipette. Discs holding experiment substances were placed on the nutrient agar media consistently seeded by the test organism, idiosyncratic antibiotic discs in company with blank discs were exploited as a positive as well negative control. These plates were kept at the low temperature like 4°C for 24 hours to allow maximum diffusion. Throughout this moment in times desiccated discs drain off the water from the adjacent medium and trial samples liquefy along with the extensive of trial disc. The diffusion occurs according to the physical rule so as to manages diffusion of molecules during the agar gel. Therefore there was a steady alter of trial matters concentrations in the medium adjoining disc [10].

Results and Discussion

From the succeeding Tables 3 & 4, this can examine to absorbance of Ceftazidime enhances with enhancing the concentration in keeping with the Beer Lambert's equation. From Table 5, it can monitor that absorbance of Ceftazidime is different and it interacts with $Mg(OH)_2$. From Table 6, it can monitor that interaction between the drug and also metal may guide to form complexes which have dissimilar light absorption ability and spectrum pattern is also altered. So any change and spectrum actions is regarded as the tool for primary contact from spectral studies. Outcome of the metals on Ceftazidime by Job's technique of incessant variation: Molar proportions of the complexes of metal salt were computed approximately through the Job's method. The examined absorbance speeds were calculated in pH 7.4 at varied concentration such as 1×10^{-5} to 9×10^{-5} Molar of Ceftazidime by metal. Then the Job's plots at pH were needed through plotting absorbance difference against mole part of drug (Table 7). From above we can monitor that Ceftazidime forms the strong 1:1 complexes with the zinc sulfate hepta hydrate which is designated as the inverted 'V' shaped curve

(Table 8). From above we can monitor that Ceftazidime forms the strong 1:1 complexes with the $Mg(OH)_2$ which is designated as the inverted 'v' shaped curve (Table 9).

Table 3: Standard curve of Ceftazidime.

$M \times 10^{-5}$	Absorbance
1	0.674
2	0.682
3	0.696
4	0.705
5	0.718
6	0.725
7	0.732
8	0.741
9	0.746

Table 4: Absorbance of Ceftazidime at different wavelength.

Wavelength	Absorbance
200	0.139
240	0.141
280	0.441
320	0.281
360	0.208
400	0.131
440	0.136
480	0.167
520	0.19
560	0.197
600	0.227
640	0.238

Table 7: Values of job's plot of Ceftazidime with $ZnSO_4 \cdot 7H_2O$.

Concentration of Ceftazidime $M \times 10^{-5}$	Absorbance of Ceftazidime	Concentration of $ZnSO_4 \cdot 7H_2O$	Absorbance of $ZnSO_4 \cdot 7H_2O$	Absorbance of mixture	Absorbance difference
	A	$M \times 10^{-5}$	B	C	$D = (A+B) - C$
1	0.674	9	0.289	0.212	0.751
2	0.682	8	0.288	0.21	0.76
3	0.696	7	0.289	0.21	0.775
4	0.705	6	0.29	0.213	0.782
5	0.718	5	0.291	0.212	0.797
6	0.725	4	0.294	0.229	0.79
7	0.732	3	0.283	0.226	0.789
8	0.741	2	0.281	0.237	0.785
9	0.746	1	0.279	0.251	0.774

Table 5: Spectral analysis of Ceftazidime with $Mg(OH)_2$.

Wavelength/nm	Absorbance of Ceftazidime	Absorbance of Ceftazidime with $Mg(OH)_2$
200	0.139	0.645
240	0.141	0.878
280	0.441	0.764
320	0.281	0.425
360	0.208	0.284
400	0.131	0.194
440	0.136	0.237
480	0.167	0.249
520	0.19	0.271
560	0.197	0.28
600	0.227	0.291
640	0.238	0.295

Table 6: Combined Spectral analysis of Ceftazidime with $ZnSO_4 \cdot 7H_2O$.

Wavelength/nm	Absorbance of Ceftazidime	Absorbance of Ceftazidime with $ZnSO_4 \cdot 7H_2O$
200	0.139	0.444
240	0.141	0.778
280	0.441	0.663
320	0.281	0.324
360	0.208	0.183
400	0.131	0.193
440	0.136	0.206
480	0.167	0.217
520	0.19	0.232
560	0.197	0.249
600	0.227	0.261
640	0.238	0.265

Table 8: Values of Job plot of Ceftazidime and $Mg(OH)_2$.

Concentration of Ceftazidime $M \times 10^{-5}$	Absorbance of Ceftazidime A	Concentration of $Mg(OH)_2$ $M \times 10^{-5}$	Absorbance of $Mg(OH)_2$ B	Absorbance of mixture C	Absorbance difference $D=(A+B)-C$
1	0.674	9	0.192	0.216	0.65
2	0.682	8	0.188	0.214	0.656
3	0.696	7	0.195	0.22	0.671
4	0.705	6	0.198	0.22	0.683
5	0.718	5	0.205	0.222	0.701
6	0.725	4	0.199	0.234	0.69
7	0.732	3	0.194	0.238	0.688
8	0.741	2	0.187	0.249	0.679
9	0.746	1	0.185	0.264	0.667

Table 9: Combined absorbance of drug with different metal and antacid.

Ceftazidime	Ceftazidime with $ZnSO_4 \cdot 7H_2O$	Ceftazidime with $Mg(OH)_2$
0.674	0.289	0.192
0.682	0.288	0.188
0.696	0.289	0.195
0.705	0.29	0.198
0.718	0.291	0.205
0.725	0.294	0.199
0.732	0.283	0.194
0.741	0.281	0.187
0.746	0.279	0.185

Table 10: Diameter of the zone of inhibition.

Bacteria Used	Standard Disk (Zone of Inhibition/mm)	Sample Disk (Zone of Inhibition)
Staphylococcus aureus	16 mm	Ceftazidime + $ZnSO_4 \cdot 7H_2O$
		14mm
Staphylococcus aureus	16 mm	Ceftazidime with $Mg(OH)_2$
		15mm

Antimicrobial Reading

The antimicrobial efficiency of the trial representatives is calculated via their action to pass up the enlargement of the microorganisms neighboring recordings which provides the clear region of inhibition. Past incubation, the antimicrobial acts of the testing materials were finished through the measuring diameter of the zones of embarrassment inside millimeter throughout a very clear mm scale. The trial models were examined also in opposition to the Staphylococcus aureus. The typical Ceftazidime disk checked also in opposition to the Staphylococcus aureus. The outcomes of antimicrobial action, computed considering diameters of the zone of inhibition in mm were revealed in Table 10. Antimicrobial feeling testing of Ceftazidime against the Staphylococcus aureus later than interacting with the $ZnSO_4 \cdot 7H_2O$ and also $Mg(OH)_2$ solution correspondingly.

Now it has proved that the zone of the inhibition of Ceftazidime with Metal and also antacid Zn, Mg diminished from the 16 mm to 14 mm and 15 mm correspondingly owing to the metal, used antacid and also drug interaction.

Conclusion

The classy spectrophotometric technique is very easy, straight in addition to worthwhile for fortitude of the drugs. Commencing this spectral interpretation, this has also been observed that Ceftazidime provides the pointed peak at 500 nm. At what time the Zinc Sulfate additionally antacid solution like $Mg(OH)_2$ merged with Ceftazidime 1:1 ratio and also the strong point of peak alters tremendously and absorption characteristics are also changed owing to the interaction even though the position of the complex do not alter. Then the antimicrobial analysis of an intermediary is very crucial to observe its spectrum in opposition to a variety

of natures of pathogenic microorganisms. The Job's plot also have provided molar fraction of the complexes of Ceftazidime through the Zinc Sulfate as well as antacid solution such as $Mg(OH)_2$. At pH 7.4 Ceftazidime structures sturdy 1:1 complexes throughout Zinc Sulfate plus antacid solution similar to $Mg(OH)_2$ assigned as 'Λ' shaped curves. These curves also can indicate the well-built kinetics of complexation between Ceftazidime by the Zinc Sulfate in company with antacid solution similar to magnesium hydroxide. The trial models were checked also in opposition to the *Staphylococcus aureus*. The typical Ceftazidime disk also ensured in opposition to the *Staphylococcus aureus*. It was also examined that the antimicrobial action of Ceftazidime reduces and it structures complexes throughout $ZnSO_4 \cdot 7H_2O$ as well as antacid solution similar to magnesium hydroxide. Thus, by the antimicrobial assessment, it was established that the zone of inhibition of the Ceftazidime with Metal and also antacid Zn, Mg diminished from the 16 mm to 14 mm and 15mm respectively.

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