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Research Article

Antibiotic with Essential Metals Complexation and Interaction, An in Vitro Study by Spectrophotometric Method

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Abstract

The present research work describes of interaction and complexation studies of Amoxicillin with essential metal & antacid and also investigation of antimicrobial activity of Amoxicillin. Amoxicillin included the third generation drug of penicillin. In vitro analysis, Amoxicillin must be interacted with metal like Mg^{2+} and Mn^{2+}. At pH 7.4, this study was performed in different ratios of Amoxicillin with metal and antacid both at room temperature 250 0C. by this study, it is investigated that drug Amoxicillin is complexed with metal as well as antacid which is confirmed by job's plot. This experiment was carried out by using ultra violet spectrophotometer. The microbial sensitivity test is important to know whether there is any change in the effectivity of Amoxicillin after the interaction with metals. There was a remarkable change in the effectivity of Amoxicillin and its complexes. This research work confirms that there was interaction between Amoxicillin with Metals like Mg^{2+} and Mn^{2+} which was confirmed by Job's plot method by spectrophotometric assay.

Keywords: Amoxicillin; Complexation; Interaction; Job's plot

Introduction

A drug interaction is said to occur when the effects of one drug are changed by the presence of another drug, herbal medicine, food, drink or by some environmental chemical agent. These unwanted and unsought-for interactions are adverse and undesirable but there are other interactions that can be beneficial and valuable, such as the deliberate co-prescription of antihypertensive drugs and diuretics in order to achieve antihypertensive effects possibly not obtainable with either drug alone. The mechanisms of both types of interaction, whether adverse or beneficial, are often very similar [1]. There are different types of drug interactions: Drug-drug interact ions, Drug-herbal interact ions, Food-drug interact ions etc [2]. Drug interactions are complex and chiefly unpredictable. A known interaction may not occur in every individual. This can be explained because there are several factors that effects the likelihood that a known interaction will occur [3]. Zinc is an important co-factor for several enzymatic reactions in the human body, vitamin B12 has cobalt atom and its core, and hemoglobin contains iron. Like Cu, Mn, Se, Cr, Mo are all trace elements, which are important in the human diet. Another subset of metals include those used in thera peutically in medicine, Al, bi, Au, Ga, Li and Ag are all part of medical armamentarium [4].

Humans need a certain amount of certain metals to function normally. Most metals are used as cofactors or prosthetics in enzymes, catalyzing specific reactions and serving essential roles. Anemia symptoms are caused by lack of a certain essential metal. Anemia can be associated with malnourishment or faulty metabolic processes, usually caused by a genetic defect [5]. The metal complexes can be utilized for the transport of selected organic chemotherapeutic drugs to target organs, or for the de-corporation of those toxic organic compounds which are able, before or after metabolic activation of reacting with metals or 1:1 complex [6]. It is emphasized that degree to which metal ions interact in vivo should employ the conditional constants which take into account competition from other ions specially Ca^{2+}, H^+ and OH^- [7]. The genotoxic consequences of the virus chemical factors involved in chelation, along with examples; kinetics, stabilization or oxidation state, lipophilicity, the mixed ligand formation, are discussed [8]. Amoxicillin is a semi-synthetic, moderate spectrum of penicillin group of antibiotics. Amoxicillin is an antibiotic that is used for the treatment of a variety of bacterial infections, skin and urinary tract infections, pneumonia, and strep throat. It binds to one of the penicillin binding proteins which inhibits the final transpeptidation step of the peptidoglycan synthesis in the bacterial cell wall, thus inhibiting biosynthesis and arresting cell wall assembly resulting in bacterial cell death [9]. Amoxicillin is a broad-spectrum antibiotic and is commonly used to treat bacterial infections of the ear, urinary tract, and upper respiratory tract [10].

Materials and Methods

In this study, all the chemical substances, reagents used here were pure and were kept under sorted under suitable conditions [11].

Preparation of stock solution [12]

In this study, 250 ml of 1×10^{-2} stock solution of Amoxicillin was measured by 0.16902 gm of Amoxicillin in 250ml of demineralized water in a 250 ml volumetric flask. This solution was further diluted to expected concentration by using buffer solution.

Preparation of metal solution [12]

In this study, 0.1M metal solution, Magnesium sulphate hepata hydrate, $MgSO_4.7H_2O$ (0.24648gm) was measured perfectly as well as the last solutions were 0.01 M concentration.

Preparation of buffer solution [12]

In this study, for the preparation of buffer solution, firstly 8.06 gm of Na_2HPO_4 was mixed in demineralized water with 1.05 gm of NaH2PO4 and then pH 7.4 was confirmed.

Preparation of standard curve of Amoxicillin [13]

In this study, Amoxicillin stock solution at pH 7.4 and concentration 1×10^{-5} M was mixed in different concentrations like: 9×10^{-5}M, 8×10^{-5} M, 7 ×10-5M, 6×10^{-5} M, 5×10^{-5}M, 4×10^{-5}M, 3×10^{-5}M, 2×10^{-5}M, 1×10^{-5}M. The absorbance volume of the solutions was determined at 256 nm by UV spectrometer.

Table 1: List of chemicals and reagents.

Sl. No.	Name	Source
1	Amoxicillin	Gift samples from alvion laboratories ltd
2	Magnesium sulfate	Merck ltd, Mumbai, India
3	Manganese sulfate	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

Table 2: List of instruments and equipment.

Name	Model	source
PH Meter	PH-211	Hanna,Romania
UV spectrophotometer	T80	PG instrument ltd, England
Electronic balance	AL-204	Mettler toleddo, Switzerland
Micropipette		Fischer scientific, Germany

All the equipment and instruments used throughout the study are given in the following table along with their source. From the above Table we can observe that the absorbance of amoxicillin increases with increasing concentration according to Beer Lambert's law. From the above Table we can observe that the absorbance of amoxicillin varies at different wavelength (Tables 1-4).

Table 3: Standards curve of Amoxicillin.

$Mx10^{-5}$	Absorbance
1	0.051
2	0.068
3	0.102
4	0.118
5	0.135
6	0.184
7	0.202
8	0.237
9	0.272

Table 4: Absorbance of Amoxicillin at different wavelength.

Wavelength	Absorbance
200	1.5
210	0.87
220	0.65
230	0.25
240	0.62
250	0.79
260	0.93
270	0.65
280	0.53
290	0.007

Results and Discussion

Table 5: Spectral analysis of amoxicillin with $MgSO_4.7H_2O$.

Wavelength/nm	Absorbance of amoxicillin	Absorbance of amoxicillin + $MgSO_4.7H_2O$
200	1.5	1.3
210	0.87	0.95
220	0.65	0.91
230	0.25	0.87
240	0.62	0.62
250	0.79	0.53
260	0.93	0.49
270	0.65	0.37
280	0.53	0.031
290	0.007	0.007

From the above Table we can observe that the absorbance of amoxicillin is different when it interacts with $MgS0_4.7H_2O$. From the above Table we can observe that the absorbance of amoxicillin is different when it interacts with $MnSO_4.H_2O$. This table shows that absorbance of amoxicillin is quite different from absorbance of amoxicillin and metal complexes (Table 5). The intensity of the peak of amoxicillin changes remarkably i.e. absorption characteristics are altered due to interaction, but the position of the compound does not shift. Interaction between drug and metal may lead to form complexes which have different light absorption capacity and spectrum pattern is altered.

Effect of metals on Amoxicillin by Job's method of continuous variation

The molar ratios of the complexes of amoxicillin with metal salts were estimated by job's method of continuous variation. The observed absorbance values were measured in pH 7.4 at various concentration (1×10^{-5} to 9×10^{-5}M) of amoxicillin and metal salts at 2310 nm. The Job's plots at pH 7.4 were obtained by plotting absorbance difference against the mole fraction of the drug (amoxicillin) which are presented in the following table. From the above table we can observe that amoxicillin forms strong 1:1 complex with magnesium Sulfate hepta hydrate which is indicated as '^' shaped curve. From the above table we can observe that amoxicillin forms strong 1:1 complex with manganese Sulfate mono hydrate which is indicated as '^' shaped curve (Table 6).

Table 6: Spectral analysis of Amoxicillin with $MnSO_2.H_2O$.

Wavelength/nm	Absorbance of amoxicillin	Absorbance of amoxicillin + $MnSO_4.H_2O$
200	1.5	0.88
210	0.87	0.84
220	0.65	0.63
230	0.25	0.52
240	0.62	0.77
250	0.79	0.62
260	0.93	0.32
270	0.65	0.19
280	0.53	0.045
290	0.007	0.013

Combined absorbance of drug with different metal

Table 7: Values of job plot of amoxicillin and $MnSO_4.7H_2O$.

Concentration of amoxicillin $M\times10^{-5}$	Absorbance of amoxicillin A	Concentration of $MgSO_4.7H_2O$ $M\times10^{-5}$	Absorbance of $MgSO_4.7H_2O$ B	Absorbance of mixture C	Absorbance difference
D=(A+B)-C					
1	0.051	9	0.069	0.043	0.077
2	0.068	8	0.072	0.048	0.092
3	0.102	7	0.078	0.056	0.124
4	0.118	6	0.084	0.061	0.141
5	0.135	5	0.134	0.067	0.202
6	0.184	4	0.110	0.060	0.234
7	0.202	3	0.101	0.125	0.178
8	0.237	2	0.056	0.156	0.137
9	0.272	1	0.012	0.187	0.097

Table 8: Values of job plot of amoxicillin and $MnSO_2.H_2O$.

Concetration of amoxicillin $M\times10^{-5}$	Absorbance of amoxicillin A	Concentration of $MnSO_4.H_2O$ $M\times10^{-5}$	Absorbance of $MnSO_4.H_2O$ B	Absorbance of mixture C	Absorbance difference D=(A+B)-C
1	0.051	9	0.205	0.078	0.178
2	0.068	8	0.195	0.072	0.191
3	0.102	7	0.186	0.082	0.212
4	0.118	6	0.182	0.055	0.245
5	0.135	5	0.176	0.017	0.294
6	0.184	4	0.112	0.039	0.257
7	0.202	3	0.097	0.071	0.228
8	0.237	2	0.052	0.096	0.193
9	0.272	1	0.019	0.128	0.163

The above table shows that the absorbance of amoxicillin differs from the absorbance of amoxicillin + $MgSO_4.7H_2O$ and amoxicillin + $MnSO_4.H_2O$ due to interaction and complexation with antibiotic and metals (Tables 7-9).

Table 9: Combined absorbance of drug with different metal.

Amoxicillin	Amoxicillin+$MgSO_4.7H_2O$	Amoxicillin+$MnSO_4.H_2O$
0.051	0.043	0.078
0.068	0.048	0.07
0.102	0.056	0.08
0.118	0.061	0.055
0.135	0.067	0.017
0.184	0.06	0.039
0.202	0.125	0.071
0.237	0.156	0.096
0.272	0.187	0.128

Conclusion

In the present work, the interaction of an important antimicrobial drug, amoxicillin + $MgSO_4.7H_2O$ and amoxicillin + $MnSO_4.H_2O$ at 7.4 by a variety of physical method like inspection of spectral behavior, Job's method of continuous variation. From spectral study, it has been seen that Amoxicillin gives a sharp peak at 256 nm. When $MgSO_4.7H_2O$ and $MnSO_4.H_2O$ salt mixed with Amoxicillin at 1:1 ratio, the intensity of the peak changes remarkably specifically absorbance decreases. That's why absorption characteristics are altered due to interaction but the position of the compound does not shift. The Job's plot has given the molar ratio of complexes of amoxicillin + $MgSO_4.7H_2O$ and amoxicillin + $MnSO_4.H_2O$. At pH 7.4 Amoxicillin forms strong 1:1 complexes with metals $MgSO_4.7H_2O$ and $MnSO_4.H_2O$ indicated as '^' shaped curves. These curves may indicate strong kinetics of complexation between amoxicillin with $MgSO_4.7H_2O$ and amoxicillin with $MnSO_4.H_2O$. When drug individually act with metals $MgSO_4.7H_2O$ and $MnSO_4.H_2O$ curve of their absorbance are verify. By this research work, it helps in the study of selection the best dosage form for better treatment. And definitely very important in adjusting the effective dose and dose ranges.

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