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Pharmaceutical Interaction of Cephradine and Metformin HCL with Antimicrobial Activity Evaluation

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ABSTRACT

Cephradine and Metformin Hydrochloride (HCL) are commonly prescribed medications for the treatment of various medical conditions, including bacterial infections and type 2 diabetes, respectively. The co-administration of these drugs is not uncommon, particularly in patients with comorbidities. This research paper explores the interaction between cephradine and Metformin HCL. An in-depth analysis was conducted through in vitro studies. The primary objectives were to assess whether Metformin HCL has the potential to influence the pharmacokinetics of Cephradine. The results of revealed that Cephradine can indeed interact with Metformin HCL. These findings suggest that the concurrent use of Cephradine and Metformin HCL may necessitate dose adjustments or close monitoring to maintain therapeutic efficacy. It is essential to comprehend how cefuroxime and metformin HCL interact in order to maximize patient care and assure reliable and efficient treatment of diabetes and infectious disorders. This study clarifies the intricacy of medication interactions and emphasizes the value of interdisciplinary cooperation between medical specialists, such as doctors, pharmacists, and clinical pharmacologists, in order to develop customized treatment regimens that take into account both the recommended course of treatment and possible drug interactions.

KEYWORDS: *Cephradine, Metformin Hydrochloride, Interactions, Zone of inhibition, Job's plot*

INTRODUCTION

Cephradine is an antibiotic belonging to the first generation of cephalosporins. Despite its limited action against gram-negative bacteria, it is effective in treating gram-positive ones. It is used to treat simple skin infections, tonsillitis, pharyngitis, and urinary tract infections. It is available in an injectable form for surgical prophylaxis outside of the United States. Drug-drug interactions are typically what first comes to mind. Drug-food interactions, drug-herb interactions, and other interactions can also occur, though less frequently. Foods containing tyramine should not be consumed by anyone taking antidepressant medications such monoamine oxidase inhibitors. A hypertension crisis could happen (as an illustration of a drug-food combination). Such cases may result from unintentional use or insufficient awareness of the drug's active components. [1] In vitro, or outside the body, drug interactions can also occur.

A couple of well-known instances include the fact that benzylpenicillin and heparin should not be mixed together, as well as thiopentone and suxamethonium. [2] Drug interactions should generally be avoided because they could have unfavorable effects. Drug interactions have, however, been utilized on purpose, such as when probenecid and penicillin were given together before penicillin was produced in large quantities. Because it was challenging to produce penicillin, it was important to discover a means to lower the dosage needed. Over a course of therapy, probenecid slows penicillin excretion. The concurrent administration of carbidopa and levodopa (sold as Carbidopa/levodopa) is a modern example of a medication interaction being used to an individual's advantage. Parkinson's disease is treated with levodopa, which must enter the brain unmetabolized in order to be effective. [3] Levodopa is metabolized in peripheral tissues outside the brain when administered alone, which reduces the drug's effectiveness and raises the possibility of side effects. The co-administration of carbidopa and levodopa, however, enables for more levodopa to enter the brain unmetabolized and also lowers the risk of side effects since carbidopa inhibits the peripheral metabolism of levodopa. [4]

Different pathways may lead to drug interactions. These procedures could result in changes to a drug's pharmacokinetics, such as changes to its Absorption, Distribution, Metabolism, and Excretion (ADME). [5] As an alternative, drug interactions may be caused by the pharmacodynamic features of the drug, such as when a receptor antagonist and agonist are administered at the same time. Cefixime is useful in managing several bacterial infections, including gonorrhea, bronchitis, and infections of the tonsils, throat, ears, and urinary tract. [6]

Many bacterial infections can be treated with cephradine, a semisynthetic wide-ranging bactericidal antibiotic. [7]

MATERIAL AND METHODS

Instruments and Equipments:

The following table lists each item of equipment and instrument utilized during the investigation, along with its source.

Table 1: List of equipment and instruments

Name	Model	Source
pH Meter	pH-211	Hanna, Romania
UV spectrophotometer	T80	PG instrument ltd, England
Electronic balance	AL-204	Mettler toleddo, Switzerland
Pipette		

Preparation methods:

a) Stock solution of Cephradine:

0.4244issolved in 100 ml buffer to prepare a 1×10^{-2} solution, further diluted as required.[8]

b) Drug solution of Metformin HCl:

0.1652issolved in 100 ml volumetric flask to obtain a 1×10^{-2} solution. [9]

c) Buffer solution:

Prepared with 2 g sodium chloride and 7 ml hydrochloric acid in demineralized water, pH adjusted to 1.75, final volume 1000 ml. [10]

Standard curve of Cephradine:

Absorbance at 254 nm was measured using UV spectrophotometry with phosphate buffer (pH 1.75) as reference. Plotting absorbance versus concentration produced the calibration curve.[11]

Images of the Sample Preparation:

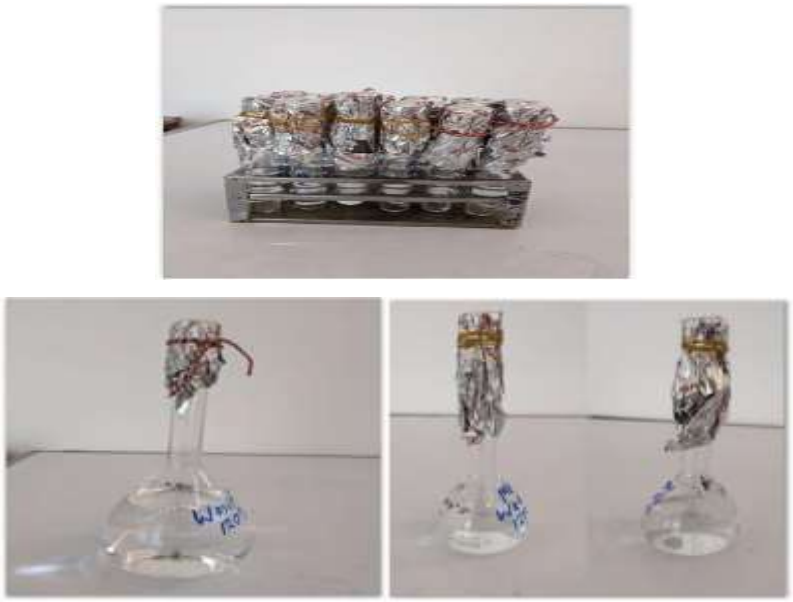

Figure 1: sample preparation

RESULT & DISCUSSION

Table 2: Standard Curve of Cephradine

M x 10^{-5}	Absorbance
1	0.461
2	0.511
3	0.545
4	0.594
5	0.634
6	0.676
7	0.726
8	0.765
9	0.799

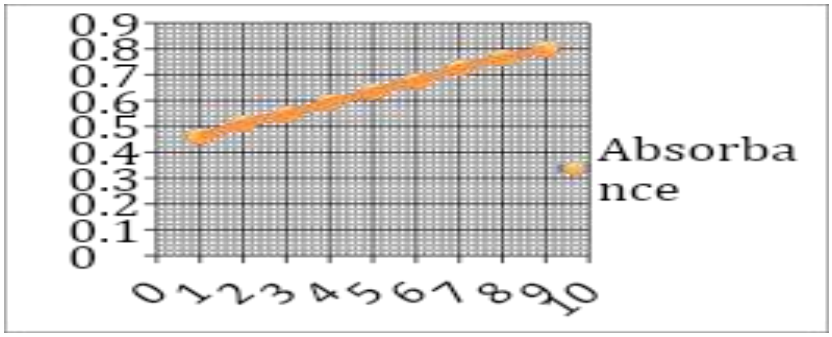

Figure 2: Standard curve of Cephradine

From the above figure, we can observe that the absorbance of Cephradine increases with increasing concentration according to Beer Lamberts Law.

Table 3: Absorbance of Cephradine at different wave length

Wavelength	Absorbance
200	**0.0111**
225	**0.0133**
245	**0.0211**
265	**0.4205**
285	**0.2083**
305	**0.2219**
325	**0.2143**
345	**0.1992**

Figure 3: Absorbance of Cephradine at different wavelength (x-axis indicates wavelength, y-axis indicates absorbance)

From the above figure, we can observe that the absorbance of Cephradine varies at different wavelength.

Spectral analysis of Cephradine with Metformin HCl

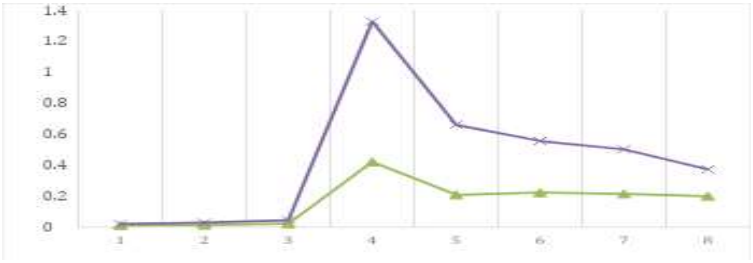

Figure 4: Spectral plot of drug and drug with Metformin HCl(x-axis indicates wavelength, y-axis indicates absorbance)

From the above figure we can observe that the absorbance of Cephradine is different when it interact with Metformin HCl.

Effect of Drug on Cephradine by Job's method of continuous variation:

The molar ratios of Cephradine-drug complexes were determined using Job's method of continuous variation. At a wavelength of 254 nm, absorbance values of cephradine and metformin HCl at different doses (ranging from 1×10^{-5} to 9×10^{-5}) were measured at pH 1.75. Plotting the variation in absorbance against the mole fraction of cephradine produced Job's plots at pH 1.75. The following table displays the findings.

Table 4: Values of job plot of Cephradine and Metformin HCl:

Concentration of Cephradine 5×10^{-5}M	**Absorbance of Cephradine A**	**Concentration of Metformin HCl 5×10^{-5}M**	**Absorbance of Metformin HCl B**	**Absorbance of mixture C**	**Absorbance difference D=(A+B)-C**
1	0.461	9	0.851	0.484	0.828
2	0.511	8	0.743	0.486	0.768
3	0.545	7	0.715	0.524	0.736

4	0.594	6	0.697	0.566	0.726
5	0.634	5	0.682	0.462	0.854
6	0.676	4	0.665	0.642	0.699
7	0.726	3	0.653	1.096	0.283
8	0.765	2	0.647	0.851	0.561
9	0.799	1	0.333	0.854	0.278

Job plot of Cephradine and Metformin HCl

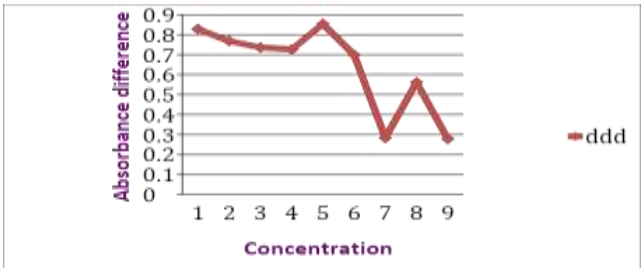

Figure 5: Absorbance difference of Cephradine and Metformin HCl

The results indicate that Cephradine forms strong 1:1 complexes with Metformin HCl, represented by a characteristic '∧'-shaped curve, confirming drug–drug interaction.

Antimicrobial Investigation

Disk diffusion method: [12]

Antibiotic-impregnated disks placed on bacteria-inoculated agar release the drug through radial diffusion, creating a concentration gradient—highest near the disk and gradually decreasing outward. Where the antibiotic concentration falls below the minimum inhibitory level, bacterial growth resumes. If the antibiotic is effective, a clear zone or ring of inhibition forms around the disk after incubation.

The antimicrobial activity of the test samples was evaluated against Escherichia coli and Staphylococcus aureus.

Table 5: The diameter of the inhibition zones, measured in millimeters, is presented in the following

Bacteria used	Standard disk (zone of inhibition/mm)	Sample disk (zone of inhibition)
Staphylococcus aureus	14mm	Cephradine
		9 mm
Staphylococcus aureus	14mm	Cephradine+Metformin HCl
		No zone of inhibition
E.coli	14mm	Cephradine+Metformin HCl
		No Zone of Inhibition

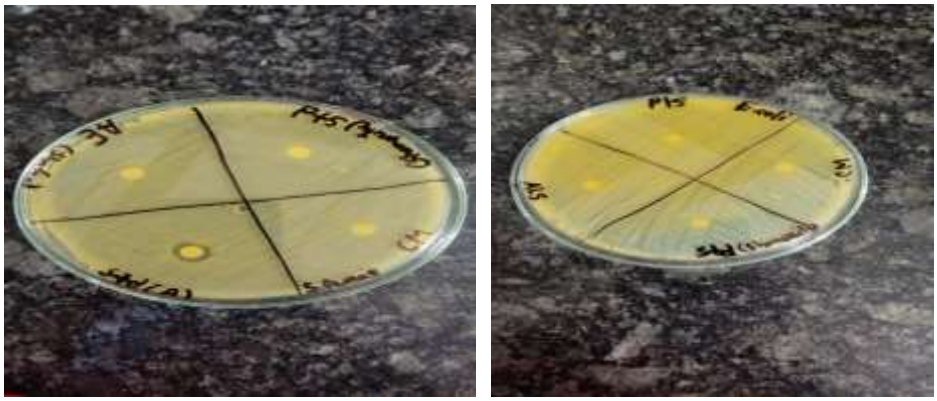

Figure 6: Disk diffusion method (C= Drug (Cephradine), C+M =Drug + Metformin HCl)

CONCLUSION

This research work confirms the possibility of a Cephradine and Metformin HCl interaction. This research work has been done by two methods one by UV spectroscopic method and another one by antimicrobial study.For the UV spectroscopic method, the standard curve for Cephradine and Metformin HCl is prepared and their absorbance vs concentration curve is almost linear means the absorbance is increased with increasing their concentration. After that the spectrum curve of Cephradine is measured at a different concentration from 200-345 nm then this spectrum of Cephradine compared with the spectrum of Cephradine+Metformin HCl

mixture, Cephradine spectrum curve is quite different from each other. From these spectrum differences, we would primarily guess there is a possible interaction between Cephradine and Metformin HCl, which will be proved via jobs plot in the next stage. In the jobs method, a vital method for this research work, it has been seen that Cephradine forms strong complexes with Metformin HCl when they are mixed at a 1:1 ratio (pH 1.75) and provides a '∧' shaped curve that confirms the interaction has occurred between Cephradine and Metformin HCl which ultimately affects the antimicrobial activity of Cefuroxime. For the Antimicrobial study, Cephradine has been tested against *E. coli* and *Staphylococcus aureus* bacteria and the test has been done via disk diffusion method. From the antimicrobial analysis, against *E. coli*, the zone of inhibition of Cephradine has reduced from 10 mm to 7 mm in case of Cephradine+Metformin HCl mixture due to their complex formation. In case of *Staphylococcus aureus* Cefuroxime shows a zone of inhibition of 13 mm while Cephradine+Metformin HCl mixture does not show any zone of inhibition.

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