SYNTHESIS, CHARACTERIZATION AND ANTIMICROBIAL STUDY OF MIXED ISONIAZID-PYRIDOXINE METAL DRUG COMPLEXES.

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ABSTRACT: Many antituberculosis metal complexes have been synthesized, but most of these drugs may encourage the bacteria that causes tuberculosis to become resistant to drugs used to treat the disease when they are taken alone and when the bacteria becomes resistant, treating the disease becomes very difficult. This has led to the research of finding a way of synthesizing more active antituberculosis drugs that the bacteria will not be able to resist. So this research was carried out in order to synthesis more active antituberculosis drug.
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1. INTRODUCTION

Tuberculosis is a disease caused by an infection called *Mycobacterium tuberculosis* which is a disease of the lungs(Behera, 2010). However, the infection can be spread through the blood from the lungs to all organs in the body. Anti-tuberculosis drugs are medicines used to treat tuberculosis. An infectious disease that can affect the lungs and other organs. Investigation of coupling a number of antituberculosis drugs under a series of conditions showed that it is possible to produce suitable antituberculosis that possess antibacterial activity. This study is aimed:

- To synthesize an alternative antituberculosis drug which will be more effective than their parent ligands.
- To characterize the synthesized complexes by determining its solubility, melting point, conductivity and infrared analysis.
- To investigate the antimicrobial activities of the complexes in order to determine the complexes with higher activities on the organisms.

2. METHODOLOGY

SYNTHESIS OF $[Cu(Py)(Iso)SO_4]$ $[Mn(Py)(Iso)Cl_2]$ and $[Cd(Py)(Iso)SO_4]$ COMPLEXES.

Procedure described by Obaleye et al., 2009 was used to synthesized this complexes. 5mmol of the solution of the metal salts used were dissolved in a beaker containing 20ml of their suitable solvents and solution of 5mmol of the ligands were also dissolved in a beaker containing 20ml of their suitable solvents. The solutions were mixed together. Immediately there was formation of precipitate. The results obtained were washed and dried. They were kept in a sample bottle for analysis.

SYNTHESIS OF $[Fe(Py)(Iso)Cl_2]$ $[Zn(Py)(Iso)SO_4]$ and $[Co(Py)(Iso)Cl_2]$ COMPLEXES.

5 mmol of the metal salts used were dissolved in a beaker containing 20ml of their suitable solvents and 5mmol of the ligands were also dissolved in a beaker containing 20ml of their suitable solvents. The solutions were mixed together and refluxed for 5 hours but no precipitate were formed. The refluxed solution were and left for 5 weeks. A dried precipitate obtained were washed and dried. They were kept in a sample bottle for analysis

3. Antimicrobial screening

Some bacterial species (*Staphylococcus aureus, Pseudomonas aureginosa, Klebsiella pneumonia,* and *Escherichia coli*) were collected from the Microbiology laboratory of the University of Ilorin Teaching Hospital (UITH.).7g of nutrient agar was measured into 250ml of sterilized water and the mixture was heated for about 15minutes and placed in an autoclave to sterilize for about 24hours. The agar was poured into some sterilized petri dish and allowed to set; the bacterial species were applied on the surface of the agar using sterilized cotton swab stick. Holes were then drilled in the middle of the petri dishes by the use of sterilized cork borer, varying concentrations of 20ppm, 40ppm, 50ppm and 100ppm of the complexes were dissolved in appropriate

solvents, and administered into the hole. The petri dishes were then incubated for close to 24hours. After incubation, the effect of the various complexes on the various organisms were measured by calculating the zone of inhibition.

4. RESULTS

Table 1: Analytical data of some mixed isoniazid-pyridoxine metal drug complexes:

Complexes/ ligand	Melting point (^oC)	Conductivity $\Omega^{-1}cm^{-1}$	TLC (Rf)
Isoniazid	169-170	-	3.90
Pyridoxine	165-168	-	3.20
[Mn(Py)(Iso) Cl_2]	180-182	5.25	3.80
[Co(Py)(Iso) Cl_2] Cl_2]	190-192	5.06	5.70
[Cu(Py)(Iso) SO_4]	204-206	5.21	4.65
[Zn(Py)(Iso) SO_4]	180-182	5.66	5.97
[Cd(Py)(Iso) SO_4]	240-243	5.40	6.10

Table 2: Infrared spectra of some mixed isoniazid-pyridoxine metal drug complexes:

Complexes/Ligands	υ_{O-H}	$\upsilon_{C=C}$	$\upsilon_{C=N}$	υ_{C-N}	υ_{C-C}	υ_{C-H}	υ_{N-H}	$\upsilon_{C=O}$	√M-L
Isoniazid		1660	1670	1062	1222	2920	3421	1725	-
Pyridoxine	3620	1626	1645	1089	1330	2895			-
[Co(Iso)(Py)Cl_2	3650	1654	1690	1039	1215	2910	3396	1710	750
[Cd(Iso)(Py)SO_4	3638	1653	1690	1020	1068	2864	3333	1710	704
[Cu(Iso)(Py)SO_4	3649	1625	1670	1066	1016	2850	3385	1716	757
[Mn(Iso)(Py)Cl_2	3634	1654	1630	1066	1089	2945	3305	1732	778
[Zn(Iso)(Py)SO_4	3649	1668	1635	1064	1043	2881	3475	1716	798

Table 3: Antimicrobial study of some mixed isoniazid-pyridoxine metal drug complexes:

Cd(Iso)(Py)(SO_4)	Zn(Iso)(Py)(SO_4)	Cu(Iso)(Py)Cl_2	Co(Iso)(Py)Cl_2	Mn(Iso)(Py)Cl_2	Pyridoxine	Isoniazid	Concentration (ppm)	Complexes/ Ligands
35	43	0	50	0	0	0	20	***Escherichia Coli (mm) (+ve)***
55	25	24	25	35	13	0	40	
12	12	38	0	51	4	0	50	
10	18	0	34	45	0	0	100	
14	44	43	42	60	0	0	20	***Staphylococcus aureus (mm) (-ve)***
25	15	9	27	22	5	0	40	
0	20	10	0	0	3	10	50	
45	6	65	0	30	13	0	100	
0	17	8	0	23	0	5	20	***Klebsiella pneumonia (mm)(-ve)***
0	5	36	2	20	0	0	40	
19	8	45	8	45	1	2	50	
43	30	9	8	60	0	0	100	
12	6	12	1	24	0	0	20	***Pseudomonas aureginosa(mm) (-ve)***
4	31	18	1	54	0	0	40	
20	6	46	0	0	0	0	50	
12	42	39	0	0	0	0	100	

5. DISCUSSION

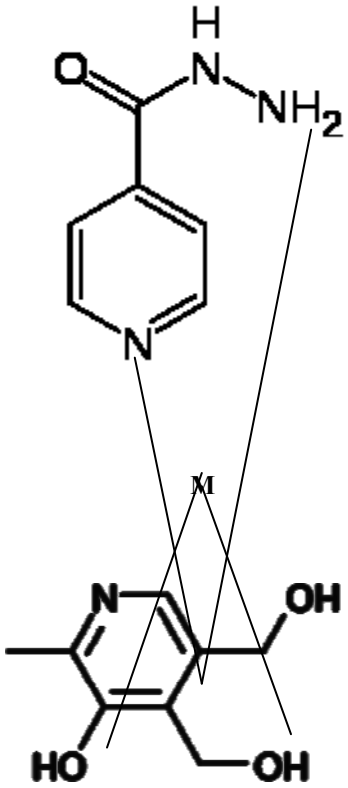
The analytical data obtained are shown in Table 1. The melting point of the ligands is higher than their parent ligands which indicates formation of the complexes(Anthony et al., 1969). From the results obtained in conductivity measurements, it was observed that the complexes are non-electrolyte(Cramer et al., 1984). Single spots were found on the Thin Layer Chromatography plate. This indicates that complexes are pure(Obaleye et al., 1993).

The IR infrared spectra of the ligands and the complexes were compared in table 2. From the result, in Isoniazid , it

was observed that coordination of the metal to ligands occurred through the nitrogen of the amine group and pyridine group. In vitamin B_6, Coordination occur through the oxygen of the hydroxyl group and nitrogen of the pyridine group(Mosset et al .,1978).

From the antimicrobial screening result of the complexes and the ligands in table 3, it could be seen that the complexes possess higher activity on some of the organisms than their parent ligands, this indicates that the complexes are more active on some of the organisms than the ligands.

PROPOSED STRUCTURE OF MIXED ISONIAZID-PYRIDOXINE METAL COMPLEXES



CONCLUSION

The new alternative drugs obtained, confirmed that they are more effective than their parent ligands. From the results obtained in infrared spectra, it was revealed that the complexes are tetrahedral in nature.

From the tests conducted on the synthesized complexes, it was observed that some of the complexes possess some antimicrobial activity, which implies that some of the complexes are more active than the parent ligands.

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