MIXED SULPHANILIC ACID - PHTHALIC ANHYDRIDE METAL DRUG COMPLEXES: CHELATION, PHYSICO-CHEMICAL ANALYSIS AND ANTIMICROBIAL ACTIVITY

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ABSTRACT

Five metal complexes of mixed sulphanilic acid-phthalic anhydride were synthesized using standard methods. They were characterized by some analytical spectroscopic techniques including conductivity measurement, elemental analysis, infrared spectroscopy, atomic absorption spectroscopy, magnetic moment and thermal studies. The ligands act as bidentate. The conductivity measurements, which were within the range of 12-20 Ω^{-1} Cm^{-1} Mol^{-1}, indicated that the complexes were electrolytes. Based on the magnetic moment and the thermal analysis, the complexes were found to be in octahedral geometry. Regions within 3400–3500 cm^{-1} in the complexes confirmed the presence of crystallization water. Bands at 500-650 cm^{-1} were attributed to the modes of vibration (M–L). Coordination occurred through the oxygen of the sulphone group and nitrogen of the amine group. In pthalic anhydride, binding site occurred at the oxygen of the carbonyl group and oxygen of the C-O group. The complexes were screened and evaluated for antimicrobial activity against some isolated organisms. From the results, the complexes were found to be more potent and active than their parent free ligands. This research work helped to produce more potent drugs which will be resistant to the organisms.

Keywords: Characterized, phthalic anhydride, sulphanilic acid, synthesized.

INTRODUCTION

Chemotherapy is very important for the treatment and management of infections [1]. When some chemotherapeutic drugs are in compounds, they exhibit toxicological and pharmacological properties [2]. Globally, complexes are known as drug designs. Some drugs in market such as Cisplatin [3] are complexes. One of the methods in obtaining new drugs is by synthesizing them which will enhance their effectiveness [4-7]. Presence of metals in drugs has helped to increase

or enhance the effectiveness of the drugs [8]. From previous research, it has been known that the ligands with different metal ions in a compound exhibit different biological properties [9, 10]. Some complexes have been screened for their antimicrobial and anticancer properties [11]. Incorporation of metal ions helps to increase the effectiveness of many drugs. [12]. They play some important role in several ways in biological processes and in the health of the organisms [13-16]. In recent researches, it has been discovered that metal ions such as copper is very useful for normal growth and function of the body system. Lack of copper causes neurodegenerative disease [17-24]. From literature review, no work has been done on this our present research. In this research work, five new complexes of Co(II), Mn(II), Zn(II) and Cu(II) chloride with sulphanilic acid-phthalic anhydride were synthesized. The aim of our research work is to produce some novel metal complexes, characterize the compounds by using some physicochemical techniques and screen all the compounds against some pathogenic micro-organisms.

EXPERIMENTAL

High grade purity sulphanilic acid and phthalic anhydride, used in this work were obtained from Sigma Aldrich Chemical Company, London and used without further purification. All the metal ions used for this work were obtained from British Drug House Chemical Limited Company, Poole, England. The isolated organisms used for screening of the complexes: *Escherichia coli*, *Klebsiella pneumonia*, *Pseudomonas aeroginosa* and *Staphylococcus aureus* were obtained from the Department of Microbiology, University of Ilorin Teaching Hospital, Ilorin, Nigeria.

The melting points of the ligands and their complexes were reported using Gallenkamp melting point apparatus at the Chemistry Department, University of Ilorin, Ilorin, Kwara State, Nigeria. The elemental analysis was carried out at Brunel Science Center, United Kingdom.

Atomic absorption spectroscopy of the complexes was carried out on Atomic absorption spectrophotometer at Obafemi Awolowo Ile- Ife, Osun State Nigeria. Infra-red spectroscopy was carried out at Redeemer University, Ogun State Nigeria. Conductivity measurement was performed with the use of HANNA instrument conductivity meter at the Chemistry Department, University of Ilorin. The thermal analyses were carried out and reported using Perkin Elmer Diamond instrument.

Synthesis of the complexes

A mixture of 1 mmole (0.173 g) of sulphanilic acid dissolved in 20 mL of distilled water and 1 mmole (0.148 g) of phthalic anhydride in 20 mL of distilled water were mixed together. The ligands solution was added to the solution of each (1 mmole in 20 mL of distilled water) metal ions salts (Co(II), Cu (II), Mn (II), Ni (II)) in a conical flask. The mixed solution was refluxed for 4 h and cooled using ice. After which, precipitation occurred. They were filtered, washed with distilled water to remove any unwanted particles and dried in a desiccator.

Antimicrobial activities

All the metal complexes prepared with their ligands were screened against some selected isolated organisms: *Escherichia coli*, *Klebsiella pneumonia*, *Pseudomonas aeroginosa* and *Staphylococcus aureus*. For the determination of the antimicrobial activities, the filter paper disc agar diffusion method was used. Sulphanillic acid and pthalic anhydride were used differently as standard for the screening of antimicrobial activities. Nutrient agar was used to culture the organisms. About 0.05 cm^3 of the compounds was introduced to the prepared agar media. About 1.0 cm diameter hole was punched. It was incubated for 3 days at a temperature of 37 ^oC. About 2.0 % w/v of the ligands and their metal complexe solutions were prepared using distilled water. Discs distilled water was used as the control. Zone of inhibitory were measured as the diameter around the surface of the plates containing the agar. The zone of inhibitory was determined using the following formular:

$$\% \text{ inhibition} = \frac{(A-B) \times 100}{A}$$

RESULTS AND DISCUSSION

Table 1: Analytical data of the complexes

Ligand/ Complexes	**M.wt**	**% Yield**	**Conductivity Ω^{-1} Cm^{-1} Mol^{-1}**	**μ_{eff} (BM)**	**% Found (Calculated)**			
					Metal Content	**C**	**H**	**N**
Sulphanillic Acid	173							

Pthalic acid	148							
[Co(SUL)(PHY)Cl_2.H_2O]	468	75	12	3.45	12.59 (12.61)	35.00 35.90)	2.43 (2.78)	2.99 (2.37)
[Mn(SUL)(PHY)Cl_2.H_2O]	464	45	15	4.97	11.42 (11.85)	36.75 (36.21)	2.76 (2.80)	2.99 (3.02)
[Ni(SUL)(PHY)Cl_2.H_2O]	468	60	20	1.26	12.77 (12.61)	34.98 (55.90)	2.39 (2.78)	2.54 (2.37)
[Cu(SUL)(PHY)Cl_2.H_2O]	473	50	13	2.78	13.46 (13.53)	35.76 (35.52)	2.43 (2.75)	2.65 (2.96)

Table 2: Infrared spectra of the ligands and their complexes

Ligand/ Complexes	**C=O**	**C-O**	**S=O**	**O-H**	**NH_2**	**M-L**
Sulphanillic Acid	-	-	1345	3461	3249	
Pthalic acid	1670	1475	-	-	-	
[Co(SUL)(PHY)Cl_2.H_2O]	1587	1450	1312	3458	3223	546
[Mn(SUL)(PHY)Cl_2.H_2O]	1575	1430	1334	3449	3232	650
[Ni(SUL)(PHY)Cl_2.H_2O]	1580	1435	1136	3462	3211	550
[Cu(SUL)(PHY)Cl_2.H_2O]	1540	1420	1178	3459	3219	519

Table 3: Thermoanalytical data (TG and DTG) of the complexes

Complexes	**TG_{range} /°C**	**DTG_{max} /°C**	**Mass loss % Observed**	**Assignment**
Co(II)	90-300	100	3.25	Loss of one molecule of water
	300-500	250	31.00	Loss of pthalic anhydride (L_1)
	80-400	320	36.49	Loss of Sulphanillic acid (L_2) Remaining $CoCl_2$
	400-800	>500	27.75	

Mn(II)	90-300	225	3.47	Loss of one molecule of water
	300-500	320	31.12	Loss of pthalic anhydride (L_1)
	80-400	390	37.10	Loss of Sulphanillic acid (L_2) Remaining $MnCl_2$
	400-800	>500	26.21	
Ni(II)	90-300	250	3.48	Loss of one molecule of water
	300-500	340	31.75	Loss of pthalic anhydride (L_1)
	80-400	390	37.10	Loss of Sulphanillic acid (L_2) Remaining $NiCl_2$
	400-800	500	27.97	
Cu(II)	90-300	230	3.79	Loss of one molecule of water
	300-500	345	31.39	Loss of pthalic anhydride (L_1)
	80-400	390	36.19	Loss of Sulphanillic acid (L_2) Remaining $CuCl_2$
	400-800	500	28.52	

Table 4: Antimicrobial Activity of the complexes

Ligand/ Complexes	Isolated Organisms 40 ppm			
	Escherichia coli	*Klebsiella pneumonia*	*Pseudomonas aeroginosa*	*Staphylococcus aureus*
Sulphanillic Acid	-	-	-	-
Pthalic acid	-	-	-	-
$[Co(SUL)(PHY)Cl_2.H_2O]$	30	12	26	11

[Mn(SUL)(PHY)Cl_2.H_2O]	14	17	15	18
[Ni(SUL)(PHY)Cl_2.H_2O]	26	33	23	16
[Cu(SUL)(PHY)Cl_2.H_2O]	23	16	7	29

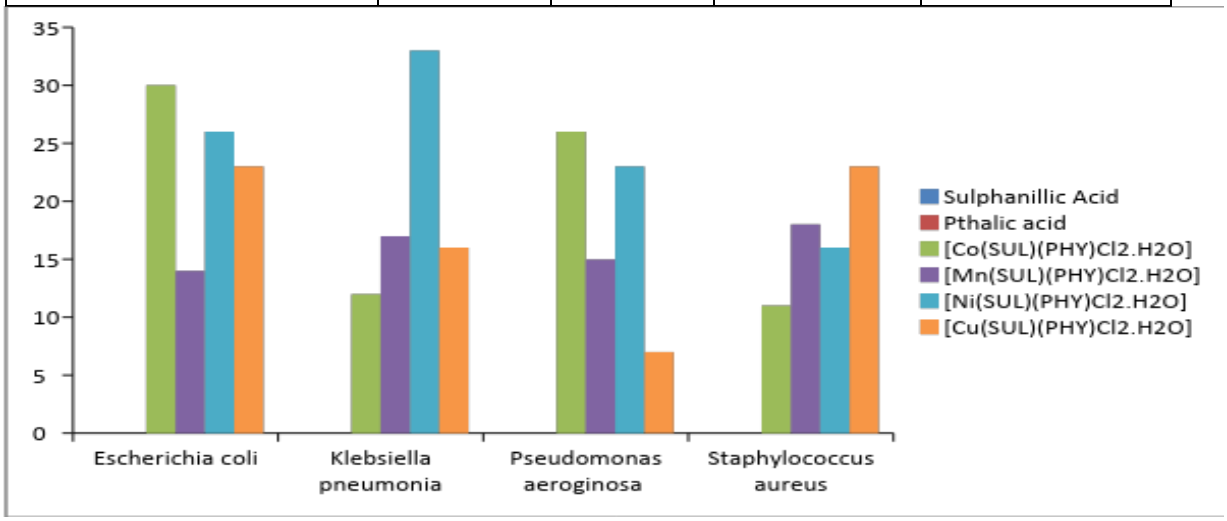

Figure 1: Graghical Representation of Antimicrobial Activity of the complexes

The analytical data of the ligands and their complexes are presented in Table 1. The results obtained from elemental analysis, confirmed the stoichiometry of the complexes and formation of the complexes. The calculated metal content and the molecular weight obtained were observed and compared with the experimental data obtained. The complexes are very stable in air. It was observed that the melting points of the complexes were higher than their parent free ligands due to the formation of the complexes. The complexes were found to be electrolytic in nature.

The IR spectra of the ligands and their complexes are presented in Table 2. Bands in the region 3400–3500 cm^{-1} in the complexes indicated the presence of crystallization water [33]. The bands at 500-650 cm^{-1} are attributed to the modes of vibration (M–L). Based on the data obtained, it was confirmed that coordination occured through the oxygen of the sulphone group and nitrogen of the amine group in sulphanillic acid. In pthalic anhydride, coordination occurred at the oxygen of the carbonyl group and oxygen of the C-O group.

All the complexes were tested with the use of $AgNO_3$ solution to determine the presence of chloride. White precipitate of AgCl was observed. This was due to the presence of chloride ion

outside the coordination sphere. The absorption bands at 1550 – 1690 cm^{-1} in pthalic anhydride were attributted to *ν*(C=O) [32]. Band at 3249 cm^{-1} present in sulphanillic acid is shifted to lower frequencies in all the complexes. This is because of the coordination of one of the terminal NH_2 in the ligand to the central metal ions [34].

The magnetic moment for Co (II) complex was 3.45 BM which indicates octahedral geometry [25, 26]. The observed magnetic moment value for the cobalt ion complex was 4.52 BM which indicates the octahedral geometry of Co(II) complex [27]. The magnetic moment for Ni(II) complex was 1.26 BM. It was observed that they show high spin. The magnetic moments of Mn(II),) and Cu(II) complexes were 4.97 BM, and 2.78 BM respectively. They corresponded to octahedral geometry [28, 29]. The thermal analyses of all the complexes are presented in Table 3. Based on the thermal curves of the complexes, there was presence of water molecules outside the coordination [30]. The ThermoGravimetric (TG) analysis of the complexes was carried out to obtain a curve using a Perkin Elmer Diamond instrument. The thermal analysis of the complexes showed that the complexes decomposed in four stages. All the complexes decomposed over time which began with the dehydration process [35-36]. Based on the observed curve, the first stage showed that one molecule of water was lost between 90-300^oC. The percentage mass loss was 3.25 which was compared with the calculated value. In the second stage, phthalic anhydride was removed within 300-500^oC with the mass loss of 31.00% which corresponde to the loss of 1 mole of phthalic anhydride. In the third stage, 1 mole of sulphanillic acid was decomposed within the range of 80-400^oC with mass loss of 36.49%. In the final stage, $CoCl_2$ remained with mass loss of 27.75% [37].

Sulphanilic acid and phthalic acid and their metal drug complexes ([Co(SUL)(PHY)Cl_2.H_2O], [Mn(SUL)(PHY)Cl_2.H_2O], [Ni(SUL)(PHY)Cl_2.H_2O],[Cu(SUL)(PHY)Cl_2.H_2O]) were evaluated for antimicrobial activity against *Escherichia coli*, *Klebsiella pneumonia*, *Pseudomonas aeroginosa and Staphylococcus aureus*. The zone of inhibition of the metal drug complexes ([Co(SUL)(PHY)Cl_2.H_2O], [Mn(SUL)(PHY)Cl_2.H_2O], [Ni(SUL)(PHY)Cl_2.H_2O],[Cu(SUL)(PHY)Cl_2.H_2O]) shown in Table 4 indicated that they were more potent or effective when compared to the parent free ligands (Sulphanillic acid and pthalic acid). This was because of their coordination which helped to reduce the polarity of the metal ions because of partial sharing of its positive charge with a donor group [35]. It also helped to increase

its lipophilic character, which subsequently favoured its permeation through the lipid layers of the cell membrane and blocking the metal binding sites on enzymes of microorganism [36]. There weree other factors which also increased the activity, such as solubility, conductivity and bond length between the metal and the ligand which may also result in facilitating the crossing through the biological membrane of the microorganisms and thereby inhibited their growth.

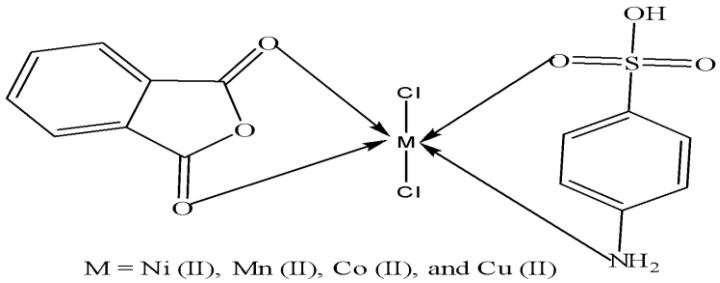

Figure 2: Proposed structure of the complexes

CONCLUSION

It has been discovered that there were some bacteria which resisted some sulphanilic drugs during chemotherapy. Since modes of action of some parent drugs are not known. It is necessary to synthesize metal drugs complexes which will be more effective than their parent drugs. In the present research, the synthesized metal drug complexes exhibited better potent properties than their parent drugs. Based on our antimicrobial results, the new metal complexes would be better therapeutic drugs for antibacterial treatment. To the best of our knowledge, we have synthesized some novel metal drug complexes which are more effective than their parent drugs.

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