COMPARATIVE SYNTHESIS, SPECTRAL AND ANTIMICROBIAL STUDIES OF METAL (II) COMPLEXES DERIVED FROM ASPIRIN

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ABSTRACT

The objective of this research work is to compare the findings of the two techniques of synthesis (solid state and solution based synthesis) in order to know whether the two results are similar or not and also to determine if the introduction of the metal ion increase or decrease the activity of the drug. From the spectral studies, it revealed that the ligand act as bidentate which coordinated to the central metal through the carbonyl of acid and ester. The elemental analysis data agreed with the proposed structure of the complexes and revealed the ratio of 2:1. Bacterial activity test shows the increase in activity from the complexes compared with the free ligand. The authors recommend the application of solid state synthesis as the method also provide the same or better result than the solution based synthesis and also the solid state method is more effective and greener synthesis.

Key words: Comparative, Solution synthesis, Solid state synthesis, Aspirin, Transition metal

INTRODUCTION

Synthetic research on complexes from ligands and transition metals have been of great interest to the chemists especially as the antimicrobial activity of the ligands (drugs) with transition metals plays important role in their complexation and their activity [1]. As many investigations have been carried out for both solution based and solid state synthesis of the ligands metal complexes as those by [2]; [3]; [4] and so on. Yusuf and coworkers in [5] defined solution synthesis as the way to synthesize new complexes by dissolving solid reactants in the solvent and refluxing the mixture using reflux condenser. While solid based synthesis which was referred as eco-friendly synthesis reported by [6] as an alternative synthetic route in which the starting materials are usually solids and the reactions are mechanically using mortar and pestle. [2] they reported the solid-state synthesis of ciprofloxacin with metal (II) in their studies and the complexes obtained were characterized using spectral, magnetic and biological studies, while in 2015 Osowale and his colleagues reported the synthesis of paracetamol using a solution-based synthesis, characterization and antimicrobial studies [7].

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Herein, the authors compare both solution and solid states synthesis results of aspirin derived metal (II) complexes, and the products obtained were characterized by comparing their spectral, magnetic and antimicrobial studies.

MATERIALS AND METHODS

Materials

Glass wares used was obtained from chemistry laboratory Aminu Saleh College of Education, Azare, metal salts and active pharmaceutical ingredient of Aspirin were purchased from sigma Aldrich and the entire chemicals was used without further purification. All glass wares, mortar and pestle were washed thoroughly after each refluxing and grinding. IR and UV/Vis spectra were recorded using FTIR spectrometer of Agilent technology in the range of 400-4000 cm^{-1} and parking palmer spectrometer lambda 35 within the range of 200-700 nm. Molar conductivity was recorded using conductivity meter of model DD-307, melting point was carried out using Stuart melting point model ISMP 101 at Bauchi State University Gadau. Antimicrobial test was carried out at the department of microbiology at Bayero University Kano.

Methods

Synthesis of the complexes [Cu $(Asp)_2$ Cl_2]

2g of Aspirin was dissolved in 10 ml of distilled water; 0.3g of sodium bicarbonate ($NaHCO_3$) was also dissolved in 10m distilled water in a separate test tube. The solution of sodium bicarbonate was added drop wise into a solution of aspirin with constant stirring until a clear solution of aspirin salt was obtained. 2g of $CuCl_2.4H_2O$ was added directly to a solution of aspirin salt with stirring. The solution was to relax for 30minutes. A green precipitate was obtained on cooling, and then the solution was filtered and dried to give Cu (II) metal complex of about 89% yield [8]. While solid state synthesis was carried out by grinding of 2g of aspirin and 1g of $CuCl_2.4H_2O$ using glass mortar and pestle for about 15minutes. The greenish powder of [Cu $(Asp)_2$ Cl_2] was obtained. The product was re-crystallized with water and filtered to give clear crystals [9]. Equation for the reaction as follows: -

$$\mathbf{CuCl_2.\ 4H_2O + 2\ (Asp) \longrightarrow [Cu\ (Asp)_2\ Cl_2]}$$

Antimicrobial Studies

Sensitivity discs were punched from Whatman no.1 filter paper, sterilized in bijou bottles by autoclaving at 121 ^{0}C for 15minutes. Sensitivity discs were prepared by taking 0.008mg of the extract or fraction and serial doubling dilution in (DMF) Dimethylformamide followed by placing the improvised paper discs in the solution such that each disc took up 0.01ml to make the disc potency of 500μg, 100ug, 200μg and 4000μg. Standardized inoculate of each isolate were swabbed on to the surface of Mueller Hinton agar in separate petri dishes and discs of the extract and standard of antibiotic (Ciprofloxacin 30μg) place. The plates were inverted and allowed to stand for 30mins for the extract to diffuse in to the

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agar after which the plates were incubated aerobically at 35 ^{0}C for 18 hours. This was followed by measurement of zone of inhibition by the test organisms around each of the extract and standard antibiotic discs [10].

RESULTS AND DISCUSSION

Solution synthesis was carried out over a long period of time and the obtained product was crystallized and filtered, solid state synthesis was carried out over a short period of time within 10-15 minutes and the product obtained is pure without further purification. The complexes gives light green colour in both methods, aspirin melted at 160^{o}C and its interactions with metal ion resulted in temperature decomposition at 170^{o}C and 166 ^{o}C in both methods as shown in table 1. The higher the values for the complexes in both methods than the free ligand revealed the good nature of the complexes and provide evidence for the coordination as revealed by the literature of [10]. The physical properties are shown in Table 1 by both methods.

Table 1: ***The physical properties of aspirin and its metal (II) complexes***

Ligand/ Compound	Methods	Colour	Melting Temperature (^{o}C)	Decomposition Temperature (^{o}C)	Conductance ($\Omega^{-1}cm^2mol^{-1}$)	Magnetic moment (BM)
Aspirin	-	White	160	-	-	-
Cu $(Asp)_2 Cl_2$	Solution based	Light green	-	170	47.0	2.10
Cu $(Asp)_2 Cl_2$	Solid state	Light green	-	166	17.0	1.90

Table 2: ***The microanalysis data of the complexes***

Compounds	Molecular formula (Molar Mass)	Methods	Microanalysis: found (calculated) %		
			C	H	M
[Cu $(Asp)_2 Cl_2$]	$C_{18}H_{16}O_8CuCl_2$ (494.9)	Solution synthesis	43.65 (44.11)	3.23 (3.35)	12.93 (13.22)
[Cu $(Asp)_2 Cl_2$]	$C_{18}H_{16}O_8CuCl_2$ (494.9)	Solid state synthesis	43.65 (42.45)	3.23 (4.36)	12.88 (13.02)

The molar conductance values of both methods as shown in Table 1, were measured in 0.001 ml in DMF which have been used to elucidate the structures of the complexes and is in the range of non-electrolyte in nature as reported by [11], the magnetic moment values of both the complexes are 2.10BM of Cu (II) complex using solution synthesis and 1.90BM using solid state synthesis

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which falls within the expected range of high spin octahedral geometry as suggested by [12].

Microanalytical data of the complexes by both methods are presented in Table 2. The % of C, H and M (M = metal ion) is in agreement with the proposed structure which revealed also, the compound by both methods [Cu $(Asp)_2 Cl_2$] as in the findings of [13].

The electronic spectra were recorded in $1x10^{-3}$ml in DMF solvent in the range of 200-700nm. The ligand showed three bands at 209nm, 227nm and 232nm which may be assigned to n- π^*, π- π^* and CT band transition which suggestive of none geometry [10]. The Cu (II) complexes by both methods showed the following λ_{max} at transitions which are summarized in Table 3 as; Cu (II) complex of solution synthesis shows three bands at 233nm, 239nm and 426nm which are assigned to n- π^*, π- π^* and ^2E_g-T^2_g, while Cu (II) complex of solid state synthesis also shows three bands at 223nm, 231nm and 327nm respectively, these are assigned to n- π^*, π- π^* and ^2E_g-T^2_g also which suggests an octahedral geometry around Cu ion as reported in the literature of [14].

Table 3: ***Electronic spectra in DMF solvent for complexes with their suggested geometry***

Ligand/ Complexes	Methods	Electronic spectra			Suggested geometry
		Wavelength (nm)	Energy (cm^{-1})	Transition	
Aspirin	-	209	47847	n- π^*	-
		227	44051	π- π^*	
		332	43103	C T	
Cu $(Asp)_2 Cl_2$	Solution based	233	42918	n- π^*	Octahedral
		239	41841	π- π^*	(oh)
		426	40650	^2E_g- E^2_g	
Cu $(Asp)_2 Cl_2$	Solid state	223	44843	n- π^*	Octahedral
		231	43290	π - π^*	(oh)
		327	30581	^2E_g- T^2g	

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Table 5: ***IR spectral data of ligand and its complexes by both methods***

Ligand/ Complexes	Methods	υ (C-O) cm^{-1}	υ (O - H) cm^{-1}	Carbonyl of carboxylate (C=O) cm^{-1}	Carbonyl of ester (C=O) cm^{-1}	M-O	M-Cl
Aspirin	-	1254-26	3372.69	1752.46	1581.71	-	-
Cu $(Asp)_2 Cl_2$	Solution based	1222.53	3406.86	1756.82	1577.68	456.00	758.39
Cu $(Asp)_2 Cl_2$	Solid state	1291.22	3312.58	1756.54	1681.41	426.60	701.24

The IR data of the aspirin and its complexes are reported in Table 4. The IR data of metal complexes behaves as bidentate manner which coordinate via one of the oxygen atoms of acidic group with the displacement of hydrogen atom and carbon of ester [15], bands at 1752.46cm^{-1} and 1581.71 cm^{-1} in the spectrum of free aspirin are assigned to υ(C=O) by ester and carboxylic group after deprotonation as these shifted in different frequencies 1756.82 cm^{-1} (1577.68 cm^{-1}) and 1756.54 cm^{-1} (1681.41 cm^{-1}) for both methods. The shifted proves that these groups represent the coordination sites of aspirin after deprotonation in carboxylic group (Mustapha et al., 2014). The bands at 456.00 cm^{-1} (758.39 cm^{-1}) and 426.60 cm^{-1} (701.24 cm^{-1}) which could not be traced in the spectrum of aspirin is tentatively assigned to M-O and M-Cl stretching frequencies as shown in the Table 4. These values were consistent with the results of [15].

Table 5: ***Anti-bacterial activity test of aspirin and its metal (II) complexes by both methods***

Ligand/ Complexes	Methods	Concentration (µg/ agar-well)	S. Aureus (mm)	E. Coli (mm)
Aspirin	-	4000	15	13
		2000	17	9
		1000	10	7
		500	8	-
Cu $(Asp)_2 Cl_2$	Solution based	4000	16	11
		2000	14	10
		1000	12	8
		500	9	7
Cu $(Asp)_2 Cl_2$	Solid state	4000	17	14
		2000	15	11
		1000	13	10
		50	12	9

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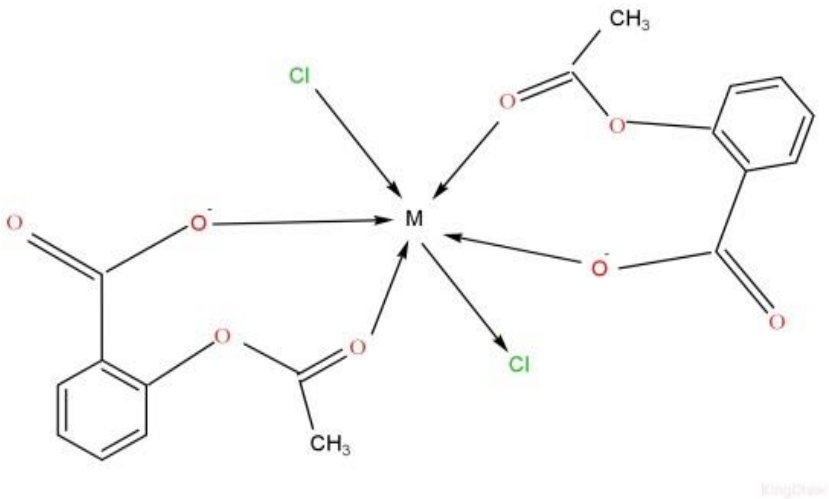
The results as presented in Table 5 shows that aspirin is active against all the bacteria isolates in all concentrations except in E. coli at 500 μg, while the complexes from both methods showed an increase in the activity than the free ligand of aspirin and are compared with the standard of ciprofloxacin as reported by [16].

CONCLUSION

From the values obtained with both methods the results are very similar in comparison. Therefore, the research work demonstrated the use of solid state synthesis for the synthesis of metal (II) complexes of active pharmaceutical ingredient of drugs. Based on the obtained values for both complexes the metal ion is coordinated to free aspirin through the carbonyl group of ester and carboxylate [10], which suggest the octahedral geometry with which UV/Vis results were consistent. Elemental analysis by both methods was consistent with the proposed structure and the 2:1 ligand to metal ratio.



Proposed structure of the complexes

RECOMMENDATION

The research promotes the application of solid state synthesis of API drugs over solution based synthesis, which is environmental difficult due to over utilization of solvent. To characterize the complexes for further investigation methods such as XRD, SEM, EDX are needed. More bacteria isolates are required to test the further activity of the complexes against the isolates.

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