SYNTHESIS AND CHARACTERIZATION OF MIXED 2,2-BIPYRIDINE AND ASCORBIC ACID METAL (II) COMPLEXES

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ABSTRACT

The trend and the importance of transition metal complexes, their synthesis, characterization, and application have been on the increase due to their impact in bioinorganic and pharmaceutical fields. In this work, we report the synthesis and characterization of ternary metal complexes with mixed ligands of 2, 2 - Bipyridine (Bipy) and L - Ascorbic acid (Asco) formulated as [M(Bipy)(Asco)] Cl_2 where M represents Cu, Zn or Co. The complexes synthesized were characterized by UV – Visible, Infrared spectroscopy, Atomic Absorption Spectroscopy, conductivity measurement, solubility test in six different solvents, and melting point. As expected, the structural analysis from the spectroscopic studies confirmed 2, 2 - bipyridine as a bidentate ligand and coordinated to the metal through the pyridinic nitrogen, while L - Ascorbic acid was also revealed to be bidentate, coordinated the metal through two of the hydroxyl group. All the new complexes are proposed to possess octahedral structures.

INTRODUCTION

Several drugs are within the scope of clinical trial stage but failed due to limitations that include unacceptable pharmacokinetic abilities. This same shortcoming is experienced even in some drugs that are already in the market (Gershell and Atkins, 2003; Karaoun and Renfrew, 2015; Kola and Landis, 2004). However, drug delivery approach has been recommended as the solution to overcome this challenge (Tiwari *et al.*, 2012). In designing such a pathway, the drugs physiochemical properties have to be modified by coordinating them with transition metals (Renfrew, 2014; Thompson and Orvig, 2003). It is the formation of this coordination complexes that navigated great interest of researchers in inorganic, pharmaceuticals and medicinal chemistry to explore metal complexes and their possible medicinal applications (Ma and Moulton, 2011; Zhang, Zhu, and Chen, 2012).

Metals used as drug carrier via coordination complexes have successfully displayed both diagnostic and therapeutic properties (Lu *et al.*, 2015; Mjos and Orvig, 2014). Metal carriers used in drug delivery have proven to impact the pharmacokinetics of drugs thereby expanded the drug solubility, permeability and bioavailable with low-cost effect (Gretta C M'bitsi-Ibouily et al., 2017. Wang, *et al (*2013) studied in vitro release of metal coordinated poly-zinc-theophylline. That it provides stable circulating triiodothyronine levels in hypothyroid rats . The coordination of metal to even known drugs have greatly improved the efficiency of those drugs (Liu *et al.*, 2018; Price *et al.*, 2014; Ragheb *et al*., 2015). The enhanced aqueous solubility of drugs due to complexation with metal was also confirmed by Breda *et al*., 2009; Chang *et al.*, 2016; Ross & Riley, 1992; Shaikh, *et al*, 2007. The solubility which resulted in the permeability was accomplished through lipid membranes (Parikh, *et al*., 2010; Pinto *et al*., 2009). These metal complexes also include ruthenium complexes (Bergamo & Sava, 2011; Lentz *et al*., 2009; Gretta *et al*., 2019; Piccariello, 2013). Again, another feature that accounted for enhanced performance of metal complexes when coordinated to drugs is the fact that some metals can be used as inert structure with extended valence space accessible to ligands and drugs (Maksimoska *et al*., 2008; Scrase *et al*., 2015).

Transition metal ions that are coordinated to imine-based ligands have been in the forefront in developing DNA molecular probes (Yousef *et al.*, 2016). Metal ions are electron deficient

whereas most biological molecules such as proteins DNA and drugs are electron rich. The attraction between these opposite charges leads to a general tendency for metal ions to bind to and interact with biological molecules (Ovig, and Abrahams, 1999). The introduction of a metal ion into a biological system will be for either a therapeutic or diagnostic purpose. The efficacy of the therapeutic agent is known to be enhanced upon coordination to a metal ion (Ajibola, 1990). Drugs that are based on mixed-ligand complexation have been known to possess enhanced biological activities (Savithri *et a*l., 2018).

Bipyridine ligands are commonly used in the formation of different complexes with a general variety of transition metals. These studies are important in understanding electron transfer processes, mixed valence complexes, magnetic coupling and magnetic transition, photochemistry and owing to an extended π - system, non - covalent π interactions in biological process as can be simulated (Savithri, *et al*., 2018). Reflecting the popularity of this 2,2 bipyridine ligand design, many substituted variants of bipy have been described (Smith *et al*., 2004). Ascorbic acid is a naturally occurring organic compound with antioxidant properties, it is a white solid but impure sample can appear yellowish, it dissolves well in water to give a mildly acidic solution (Safety MSDF, 2005). Being derived from glucose, many animals are able to produce it, but human require it as part' of their nutrition (Davies *et al*, 1991). The prevalence of antimicrobial resistance among pathogenic bacteria is increasing both among hospital patients and in the community (Lachapelle and Drouin, 2010). This work reports the synthesis and characterization of mixed 2, 2-bipyridine - ascorbic acid metal complexes.

MATERIALS AND METHODS

The drugs, chemicals and solvents used in this study were of high purity and were used as purchased from Sonitex Nigeria Enterprise without further purifications. Metal (II) chlorides of Cu, Zn and Co were used.

Synthesis of the complexes

Synthesis of $[Cu(Bipy)(Asco)Cl_2].2H_2O$

The mixed ligand metal complexes were synthesized following a literature procedure described by (Adeyemo *et al*., 2004). A solution of $CuCl_2.2H_2O$ (0.51g, 0.003mole) in (30mL) distilled water was added to a 30mL warm solution of 2,2-bipyridine (0.46g, 0.003mole) in distilled water heated on water bath for 5 minutes and Ascorbic acid (0.53g, 0.003mole) in 30mL distilled water also added. The resulting mixture was stirred and heated for 1 hour, until clay coloured precipitate was formed, when there was complete precipitation the mixture was cooled to room temperature. The clay precipitate was filtered and dried at room temperature. The percentage yield was 76.00 %. The same procedure was used in the synthesis of the Co and Zn complexes.

$$CuCl_2.2H_2O + Bipy + Asco \xrightarrow[Heat]{} [Cu(Bipy)(Asco)Cl_2].H_2O$$

RESULTS AND DISCUSSION

The complexes and ligands were either soluble or slightly soluble in the various solvent when hot but were mostly not soluble in the cold solvents. All the complexes showed higher melting points compared with the individual ligands used in complex formation. All the complexes have high percentage yield in the range of 76.00-92.98. The complexes were of various colours.

Table 1: Solubility test for 2, 2-biphyridine, Ascorbic acid and metal complexes

COMPOUND	Dist. H_2O		Ethanol		Methanol		Acetone	Chloroform	DMSO	
	C	H	C	H	C	H	C	C	C	H
2, 2-bipyridine	NS	S	SS	S	S	S	S	S	S	S
Ascorbic Acid	S	S	NS	SS	NS	SS	NS	NS	SS	S
[Cu(Bipy)(Asco)Cl_2]	S	SS	NS	SS	SS	SS	NS	NS	SS	S
[Zn(Bipy)(Asco)Cl_2]	S	SS	SS	-	SS	-	NS	-	-	-
[Co(Bipy)(Asco)Cl_2]	NS	SS	SS	S	NS	S	NS	NS	SS	SS

Key: C-Cold, H-Hot, S-Soluble, SS-Slightly Soluble and NS-Not Soluble

Table 2: Analytical data of mixed 2, 2-Bipyridine and Ascorbic acid metal complexes.

Compound	Colour	Melting Point (^{0}c)	% Yield	Conductivity (µs/Cm)
2, 2-Bipyridine	White	90	-	01
Ascorbic Acid	White	204	-	29
[Cu(Bipy)(Asco)C_2]	Green	230	76.00	30
[Zn(Bipy)(Asco)C_2]	Grey	>300	97.90	37
[Co(Bipy)(Asco)C_2]	Clay	>300	92.98	01

Table 3**:** Selected IR data (cm-^{1}) of the mixed 2,2-bipyridine and ascorbic acid complexes.

Compound	V(N-H)	V(C-N)	Aromatic substituted benzene VCC-H	Aromatic V(C=C)	V(C=O) (s)	V(C=N)	Aromatic Ring (s)	V(O-H)	V(C-O) (s)	V(M-L) (s)	V(C-CL)
2,2-Bipyridine	3649.44(w)	1338.64(m,s)	3055.35 (s)	1577.82 (s)	-	1697.41(w,s)	758.05	-	-	-	-
Ascorbic Acid	-	-	3030.27 (b)	1541.18 (m)	1753.35	-	756.12	3649.44(m)	1276.91	-	-
[Cu(Bipy)Asco)Cl_2]	3354.32(m,s)	1315.50(s)	3051.49 (w)	1566.25 (s)	1600.97	1647.26 (s)	789.62	3444.98(s)	1229.91	418.57	806.27(m)
[Zn(Bipy)(Asco)]Cl_2]	3576.14	1319.35(s)	3072.71 (s)	1599.04 (s)	1716.70	1654.98 (m,s)	771.55	3576.14(m)	1251.84	414.71	819.77(s)
[Co(Bipy)Asco)Cl_2]	-	1309.71(s)	3088.14 (s)	1537.22 (s)	1604.83	1674.27 (s)	767.69	3448.84(b)	1247.99	416.64	908.50(m)

The IR spectra of 2, 2-bipyridine and its complexes were compared, and it was observed that the absorption band 1338.64 cm^{-1} due to ν(C-N) vibration in 2,2- bipyridine has shifted in the spectra of all the complexes. Similarly, the ν(C=N) band, 1694.4 cm^{-1} in 2,2-bipyridine spectrum also shifted in spectra of all the complexes.

The IR spectrum of ascorbic acid ligand was compared with its complexes, it was also observed that the absorption band 3649.44 due to ν(O-H) vibration shifted significantly in all the complexes, meaning that the H of the hydroxyl in the ligand have been substituted with a bond from the metal. There was a slight backward shift to lower frequency (from 3649.44 cm^{-1}) for V(O-H), indicating probably the presence of an attachment at the site (Simó *et al*., 2000). In the [Cu(Bipy)(Asco)Cl_2] complex, the shifts that suggested the position of attachment of the ligands to the central metal atom were more pronounced at the ν(C-N) absorption band and ν(C=N) absorption band for 2, 2-bipyridine ligand, while the ascorbic acid ligand coordination is more likely through the ν(O-H) whose band shifted significantly from a higher frequency of 3649.44 cm^{-1} in the free ligand to a lower frequency of 3444.98 cm^{-1} in the complex.

In the complexes [Zn(Bipy)(Asco)Cl_2] and [Co(Bipy)(Asco)Cl_2], the observations for the 2, 2-bipyridine and ascorbic acid ligands also showed shifts in absorption peaks that indicated possible sites; of coordination to the central metal ion were; (C=N) and (C-N) for 2, 2-Bipyridine and O-H for Ascorbic acid. Again, it is observed that in the complex [Zn(Bipy)(Asco)Cl_2], absorption band for ν(C=N) and ν(C-N) in 2, 2-Bipyridine shifted from 1697.41 cm^{-1} to 1654.98 cm^{-1} while; 1338.64 cm^{-1} to 1319.35 cm^{-1}, respectively. However, the ν(O-H) in the ascorbic acid shifted from 3649.44 cm^{-1} to 3576.14 cm^{-1} as well.

Similarly, in the [Co(Bipy)(Asco)Cl_2], absorption band ν(C=N) and ν(C-N) in 2, 2-bipyridine shifted from 1697.41 cm^{-1} to 1674.27 cm^{-1} and 1338 to 1309.71 cm^{-1}, respectively. It is also observed that the ν(O-H) in the ascorbic acid shifted from 3649.44 cm^{-1} to 3448.84 cm^{-1}. These positions indicated probable positions of attachment to the metal cemtre (Ajibade and Kolawole, 2008).

Table 4: Some selected Uv-visible spectral data for 2, 2-bipyridine, ascorbic acid and their metal complexes.

Compound	Wavelenght (nm)	Energies (kg/mol)	Assignment
2, 2-bipyridine	191.40	625.41	$\pi \rightarrow \pi^*$
	288.40	415.06	$n \rightarrow \pi^*$
Ascorbic Acid	192.40	622.16	$\pi \rightarrow \pi^*$
	282.80	423.28	$n \rightarrow \pi^*$
[Cu(Bipy)(Asco)Cl_2]	307.00	389.91	$n \rightarrow \pi^*$
	530.50	225.64	LMCT
[Zn(Bipy)(Asco)Cl_2]	282.50	423.73	$n \rightarrow \pi^*$
	668.00	179.19	LMCT
[Co(Bipy)(Asco)Cl_2]	302.00	396.37	$n \rightarrow \pi^*$
	563.50	212.43	LMCT
	232.00	515.97	$\pi \rightarrow \pi^*$
	202.00	592.60	$\pi \rightarrow \pi^*$
	232.50	514.86	$\pi \rightarrow \pi^*$

The ultraviolet spectrum of the 2, 2-bipyridine ligand showed two absorption peaks, one at 191.40 nm corresponding to energy of 625.41 kg/mol due to $\pi \rightarrow \pi^*$ transition and the other at 288.40 nm corresponding to energy of 415.06 kg/mol due to $n \rightarrow \pi^*$ transition. Comparison of electronic transitions in ligands and complexes, the [Cu(Bipy)(Asco)Cl_2], [Zn(Bipy)(Asco)Cl_2] and [Co(Bipy)(Asco)Cl_2] all undergo a $\pi \rightarrow \pi^*$ transition; there was also an $n \rightarrow \pi^*$ transition which is a bathochromic shift in spectra of all the complexes except in [Zn(Bipy)(Asco)Cl_2] that has the same $n \rightarrow \pi^*$ wavelength as in ascorbic acid spectrum since is zinc does not exhibit d-d transition though it is a d-block metal (Olajire, 2011).

The observed bathochromic shift could be attributed to a change in the compound composition due to coordination (Ajibade *et al*., 2006) as observed in the spectra of related complexes with N, N bidentate ligands (Gichumbi *et al*., 2017).
Ligand to Metal Charge Transfer (LMCT) absorption transitions were also observed in the mixed ligand complexes. These are indications of metal complex formations (Simó *et al*., 2000)

Atomic Absorption Spectroscopy
The atomic absorption spectroscopy was carried in line with the literature procedure described by (Yan *et al*., 1999) which normally relies on the Beer-Lambert's law. The analysis was run on Alpha Atomic Absorption Spectrophotometer. 100mg of each sample was digested in 8mL of 6M HCl and 0.8mL conc. HNO_3, that is double acid method.

Table 5: The atomic absorption spectral data for the metal complexes of 2, 2-bipyridine and ascorbic acid.

Metals Analyzed	Concentration (µg/g)
Copper	157.38
Zinc	186.49
Cobalt	112.76

The result from the atomic absorption spectroscopy shows that the expected metals were present in each of the complexes and in a good concentration ranging from 112.76 for cobalt, 157.38 for copper and 186.49 (µg/g) for zinc.
From the above analytical and spectroscopic data, the following structures were proposed for the complexes as shown in figure 1 below:

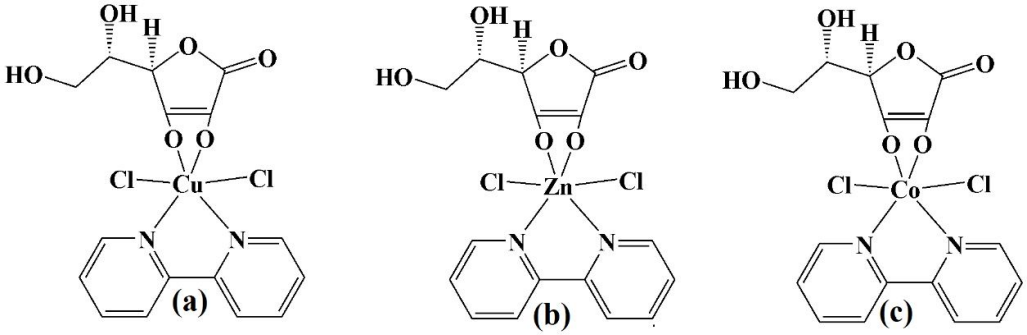

Fig 1**:** The proposed structure for (a) $[Cu(Bipy)(Asco)]Cl_2$] (b) $[Zn(Bipy)(Asco)]Cl_2$] and (c) $[Co(Bipy)(Asco)]Cl_2$] complexes.

CONCLUSION

Mixed ligand metal complexes of 2, 2-bipyridine and ascorbic acid formulated as $[Cu(Bipy)(Asco)Cl_2]$, $[Zn(Bipy)(Asco)Cl_2]$ and $[Co(Bipy)(Asco)Cl_2]$ have been successfully synthesized and characterized. As expected, the spectroscopic data confirmed 2,2- bipyridine as a bidentate ligand which coordinated the metal ions through the two pyridinic nitrogen atoms while the L- ascorbic acid coordinated the metal ion through the two oxygen of the hydroxyl groups. The electronic data confirmed a bathochromic shift in all the metal complexes due to ligand to metal charge transfer (LMCT) as a clear indication of coordination. The tentative metal - ligand (M-L) assignments from all the spectroscopic data favour six coordinationate (octahedral) structures for the complexes studied. The atomic absorption spectroscopic data of the pure compounds isolated showed the expected metals were present in the respective complexes.

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