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Synthesis and Characterization of Cu (II) Complexes of Salicylate Ligands

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ABSTRACT: This work evaluates the synthesis and characterization of Cu (II) complexes of salicylate ligands using green method. The complexes were synthesized by direct mixing of the metal salt ($CuCO_3$) dissolved in water and a corresponding ligand dissolved also in water. The complex was obtained in excellent yields (80%) by moderate heating in distilled water. The complexes were characterized by Ultra-Violet Spectrophotometer (UV-Vis), solubility, melting point and X-ray diffraction. Metal complex with formula of Cu (II)-L_2 where L = acetylsalicylic acid and salicylic acid were obtained. The ligands gave crystalline complexes as it bonds to the central metal (copper).

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Drugs are natural or synthetic substances which (when taken into a living body) affects its functioning or structure, and is used in the diagnosis, mitigation, treatment, or prevention of a disease or relief of discomfort. (cis-$[Pt(NH_3)_2Cl_2]$) which is used in the treatment of tumor was accidentally discovered by Barnett Rosenberg in the 1960s when he was studying the resemblance between the mitotic spindle of dividing cells and the orientation of iron filing around a magnetic field (Alderden *et al*., 2006; Fricker, 2007; Kiremire, 2010). The discovery and development of the antitumor compound cisplatin and its analogues played a very important role in the establishment of the field of medicinal inorganic chemistry (Fricker, 2007). Since the discovery of cisplatin there has been an upsurge in research in the field of metal-based therapeutics.

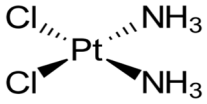

Fig 1. Structure of Cisplatin

Salicylate ligands (salH and ASA) are well-known class of drugs that are antipyretic, analgesic and anti-inflammetory agents. They are found to be among the most consumed drugs over the world and are used in clinical practice of inflammatory disorders including cancer, arthritis as well as for prevention of myocardial infarction and pain relief (Kovala *et al*.,

1998; Konstandinidou *et al*., 1998). Cu(II) complexes with aspirin and other salicylic acid derivatives have been found to be more potent and desirable drugs than their constituent ligands (Jacka *et al.*, 1983). Evidence of experimental research work by different researchers all over the world proved that the coordination of Cu(II) ion by salicylate ligands improves the potency, stability and other pharmaceutical activity of the drugs and reduce their undesired toxicity effects in human and veterinary medicine (O'Connor *et al*., 2012; Weiping *et al*., 1998).

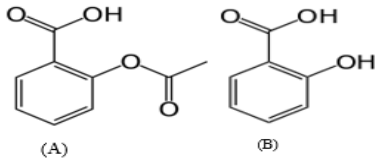

Fig 2. Structure of (a) acetylsalicylic acid and (b) salicylic acid

There is a large amount of information available on the synthesis and characterization of metal chelates derived from copper and biologically important ligands, because of the usual improvement in the biological properties of parent ligands (Abosede *et al*., 2016). However, the synthesis of these complexes has always been through non-benign routes. Therefore, the green synthesis of copper complexes of Salicylic acid (salH) and Acetylsalicylic acid (ASA) is of interest in order to evaluate their coordination chemistry and biological activity.

MATERIALS AND METHODS

Copper carbonate hydroxide, acetylsalicylic acid (ASA) and salicylic acid (salH) were obtained from commercial sources and were used without further purification. The melting points of the complexes were

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determined using Stuart melting point (SMP 11) apparatus, while solubility was determined in analytical grade solvents: methanol, ethanol, distilled water and acetone. Electronic absorption spectra were taken on JASCO V-730 Ultraviolet Visible spectrophotometer and diffraction measurement was taken on Pananalytica X'pert X-ray diffractometer.

Synthesis of complexes of [Cu (II)(ASA)] (1) Complex: Copper carbonate hydroxide (0.122 g, 1 mmol) was added to a 6 mL of hot distilled water in a round bottom flask (insoluble), set upon a heating mantle and heated for about 10 minutes. ASA (0.360 g, 2 mmol) was added to the solution in the round bottom flask and continued heating. The mixture was refluxed on a water bath for 90 minutes. Greenish solution was formed upon dissolution of ASA. A greenish resulting solid complex 1 was collected by filtration and washed with 2 mL of hot water and was kept for 3 weeks to dry (Yield: 80%). (Abosede *et al*., 2016)

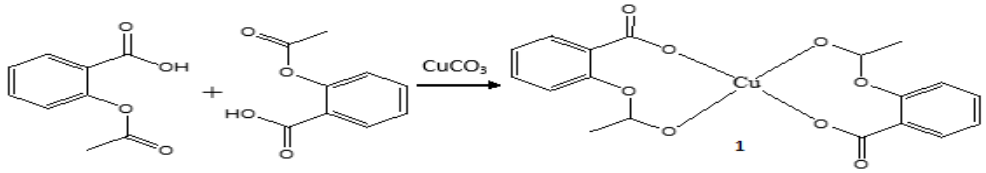

Fig 3. Schematic synthesis of [Cu (II)(ASA)] *Complex*

Synthesis of [Cu (II)(salH)$_2$] Complex (2): Copper carbonate hydroxide (0.122 g, 1 mmol) was added to a 6 mL of hot distilled water in a round bottom flask (insoluble). It was set upon a heating mantle and was heated for about 10 minutes. salH (0.314 g, 2 mmol) was added to the solution in the round bottom flask. The mixture was refluxed on a water bath for about 20 minutes. The resulting solid complex 2 was collected by filtration and washed with 2-3 mL of hot water and was kept for 3 weeks to dry. Green crystals of 2 were formed in the green filtrate after 3 weeks (Abosede *et al*., 2016).

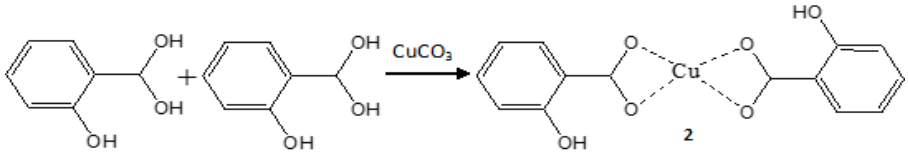

Fig 4. Schematic synthesis of [Cu (II)(salH)$_2$]

RESULTS AND DISCUSSION

The physical properties of the ligands and their metal complexes are given in Table 1. The absorption spectra of the complexes and their respective ligands were recorded in the range of 200-400 nm. The absorption spectra have been recorded in the mother liquor (water) prior to the precipitation of the isolated complexes. In aqueous solution, acetylsalicylic acid (ASA) had a single absorption peak at 275 nm while salicylic acid (salH) had two absorptions peaks at 230 nm and 297 nm due to intraligand transition (π-π^*) (Fig 5a). This absorbance was compared to that of the complexes formed. The electronic spectra of these ligands and their complexes were illustrated in Table 1.

Table 1. Physical and absorption characteristics of the ligands and copper complexes

Compound	Colour	Melting point ^oC	Appearance	Ligand transitions (nm)
ASA	White	110-130	Crystalline	275
salH	White	105-120	Crystalline	230 (sh*) & 297
[Cu(ASA)$_2$]	Green	175-180	Crystalline	296
[Cu(salH)$_2$]	Green	170-185	Crystalline	228 (sh)& 295
$CuCO_3$	Light green	> 360	Powdery	------

**sh = shoulder*

Table 2. Solubility of the ligands and metal complexes in different solvents

Compound	**Distilled Water**	**Ethanol**	**Methanol**	**Acetone**
Salicylic acid	S1S	S	S	S
Acetylsalicylic acid	S1S	S	S	S
Copper(II) carbonate	I	I	I	I
[Cu(salH)$_2$]	I	S	S	S
[Cu(ASA)$_2$]	I	S	S	S

S1S = slightly soluble; S = soluble; I = insoluble; VS = very soluble

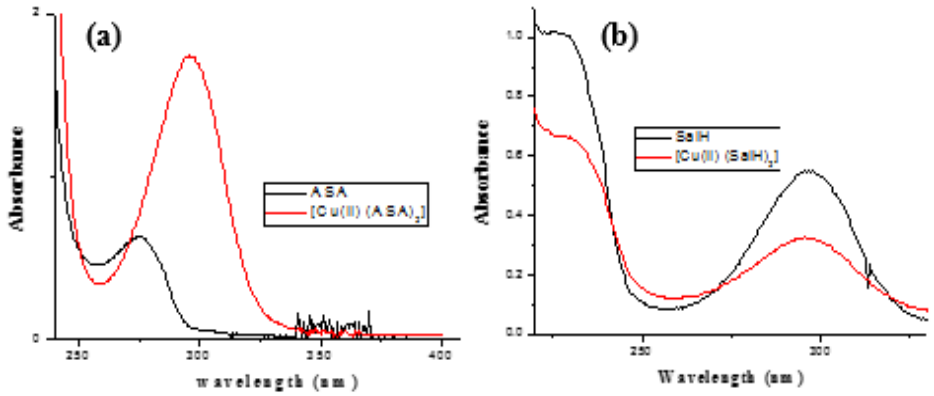

Fig 5. Absorption spectra of aqueous solution of (a) acetylsalicylic acid and its copper complex; (b) salicylic acid and its copper complex.

The solubility results show that salH and ASA are slightly soluble in water and their metal complexes are insoluble. In other solvents used in the test, the solubility of the metal complexes showed a different pattern whereby their solubility varied from slightly soluble to being soluble. The copper complex with acetylsalicylic acid had a single peak at 296 nm (Fig 5a) of the ultraviolet region, while copper complex with salicylic acid had two peaks at 228 nm and 295 nm (Fig 5b). Complexes of $[Cu(II)(ASA)_2]$ and $[Cu(II)(salH)_2]$ also showed the absorption peaks of the ligands but with shifting comparing with the ligand; ASA absorption at 275 nm appears at 296 nm in $[Cu(II)(ASA)_2]$; this corresponds to a red shift (from a lower wavelength to a higher wavelength), while salH and $[Cu(II)(salH)_2]$ had absorption at 297 nm and 295 nm; this corresponds to a blue shift (from a higher wavelength to a lower wavelength). These changes in the absorption spectra confirm that both complexes were new products from acetylsalicylic acid and salicylic acid respectively. Furthermore, the X-ray diffraction pattern of $[Cu(II)(ASA)_2]$ (Fig 6) reveal that the complex has a crystalline morphology.

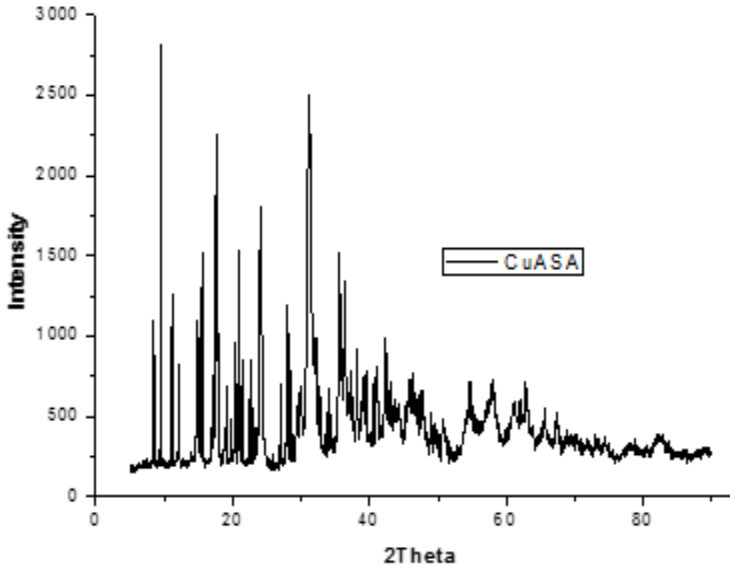

Fig 6. X-ray powder diffraction pattern of $[Cu(II)(ASA)_2]$.

Conclusion: In this research, two metal complexes of salicylic acid and its derivative (acetyl salicylic acid, aspirin) have been synthesized and characterized by UV-spectroscopy, solubility, melting point and X-ray powder diffraction (XRD). This work confirms the environmentally friendly synthesis of two metal complexes of copper *viz*: [Cu (II)$(ASA)_2$] and $[Cu(II)(salH)_2]$ with the use of non-toxic solvent, water. This synthesis method is low cost and saves time. The spectra of the ligands and the complexes formed proved that new products were formed and are stable.

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