REVIEW ARTICLE

Synthesis and characterization of Al(III) complex with paracetamol

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ABSTRACT

The complex of Al (111) with paracetamol have synthesized and characterized using UV–Vis, Infrared spectroscopies and melting point. The ligand has been found to behave as tridentate chelating agents. Paracetamol complex coordinate through the carboxylate oxygen, phenolate oxygen atom, and amine group. The complex solubility was evaluated for several solvents and it was found the compound was more soluble in DMSO. Job's method of continuous variation suggested 1 : 2 metals to ligand stoichiometry for paracetamol complex

Keywords: Aluminum, Paracetamol, Trivalent state metal complexes.

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INTRODUCTION

The word acetaminophen and paracetamol both originate from a chemical name for the compound Para-acetylaminophenol and para-acetylaminophenol C8H9NO2.[1,2]

Acetaminophen is a white solid which melts at 170 0C, soluble in water and methanol. Paracetamol is widely used without prescription as a painkiller and fever reducer.[3-5] Morse first synthesized it in 1878.[6] The discovery of paracetamol was an accident when a patient was given a same molecule (acetamide) roughly 100 years ago. However, acetamide is toxic in a mild quantity. Consequently, scientists started to alter the acedamide's structure to try and to make a new compound that possessed less toxicity but remained the integrity of its structure, and thus Acetaminophen was found.[7] Acetaminophen was prepared by reaction of p-nitrophenol with acetic acid at a free-air environment in the presence of argon atmosphere. Then thermal treatment at 230°C was performed, and it was followed by constant stirring for 15 hours.[8,9]

Previous literature review showed metal complexes of Acetaminophen have been reported.[10-12] The history of metal-paracetamol complexes began when researchers arrived at the possibility of paracetomol chaleting with some heavy metals, as Acetaminophen usually coordinate as a bidentate ligand through a hydroxyl group located on the benzene ring, forming H-O-M and a carbonyl group, producing C=O-M.[13,14] The coordination manner of C=O-M was reported for some transition metals and confirmed mostly by infrared red techniques. A good illustration of this is the formation of Copper-paracetamol complexes that were made at borate buffer in the presence of sodium nitrate.[11] The authors used Mass spectrometry and Nuclear Magnetic Radiation (NMR) to propose the product's structure and indicated the copper. is coordinated to the chelating ligand via the amine and carbonyl groups. The systemwas found to have a stoichiometric ratio of 1:1 for the metal and ligand. Lawal, A., and Obaleye reported the synthesis of Co(II), Ni(II), Fe(III) with aspirin and paracetamol.[15] These coordination compounds exhibited 1:1 ratio metal to ligand, where the Complexation was observed via OH, and C=O group. Furthermore, Aderoju a. Osowole et. studied paracetamol complexes with Copper (II) chloride tetrahydrate, Nickel(II) chloride hexahydrate, Cobalt (II) chloride hexahydrate, Manganese (II) chloride tetrahydrate, Zinc (II) nitrate hexahydrate, and Zinc (II) acetate dehydrate and percentage metal, magnetic and spectroscopic data were employed to suggest a reasonale structure.[16] It was observed that these materials gave a proposed structure with 1:2 ratio metal to ligand, where the ligand was bounded to the metals through hydroxyl and carbonyl groups.

Rakesh Choure and Neelam Vaidya reported the synthesis and analgesic effect of Zn(II)-Paracetamol complex. First, the authors made the phase through mixing an appropriate amount of Zn(II) and Paracetamol at PH 7.2. The researchers carried out a polarographic method for structural determination. Observed in this study was Zn(II) Paracetamol phase found to have a 1:1 stoichiometric ratio in which both OH- and C=O group are expectedly involved in the coordination with Zn(II).[17]

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In addition, Acetaminophen acts as a bidentate ligand via amine and carbonyl groups. Research area on this coordination form was not extensively investigated; only few metals complexes were reported.[11,18,19]

Mg (II), Ca (II), Ba (II), Sr (II) display complexes with paracetamol in which the metal connected to the ligand through the lone pair of nitrogen and the carbonyl amide unit and these phases found to have 1:2 stoichiometric ratio for the metals and the ligand.[20,21]

The biological behaviors of the complexes towards some bacterial species such as Bacillus, Serratia were also intensively examined.[4] The key factor of these compounds acting as antibiotics candidate is their increased stability and half-time.[5] The chaleting materials were also reported to have a slow metal-ligand exchange rate. This property can compete the division rate of bacteria over a period of time. Thus, this mechanism offers a good kill for the intended bacteria and decreases the number of doses taken.

While a large amount of studies have been conducted on paracetamol complexes containing divalent group II ions and transition metal ions, research on Aluminium complexes with paracetamol has not been studied. The aim of this publication is to report the synthesis, characterization of the resulting compound formed from the reactions of paracetamol with $AlCl_3$.

METHODOLOGY

Pure, white paracetamol of melting point 170°C was obtained from AL-Kendy company. A solution of Aluminium chloride was prepared by dissolving 16 mg of $AlCl_3$ in 100 mL distilled water; a solution of paracetamol was also prepared by dissolving the 15 mg of pure paracetamol sample in 100 mL of a methanolic solution. Using distilled water and methanol as the blank, the absorption of Aluminium chlorideand paracetamol were measured from to 243 nm 300 nm, respectively. The spectra was used to determine the purity of the two compounds.

Determination of stoichiometry

The stoichiometry of the formed complex was found by job's method of continuous variation. Cation and ligand solution with the same analytical concentration were added together in a fashion that the total volume in each maxiture was 10 mL. The absorbance of each solution was then measured at proper wavelength and plotted against the mole fraction of the reactants.

Synthesis of Paracetamol-aluminium Complex

The formation of Al(para)x Cl_3 was carried out as described below. The procedure started with first mixing 0.01 mol of water solution of Aluminium chloride and 0.02g of dissolved paracetamol in methanol. Dissolving and mixing processes were done at room temperature. The mixture was transferred to a water bath at 60°C with two hours stirring. After that, the rounded bottom flask along the mixture was removed from the water bath and left for three weeks for precipitant to form. After the black precipitant settled in the bottom of the flask, it was transferred to a Buchner funnel for filtration and drying.

DISCUSSION

The complex was confirmed to be stable. It was a non-hygroscopic material with a higher melting point, indicating the complex is more stable than the free ligand. The complex was black in color. To confirm the chemical structure of the complex, both IR and UV-visible light instruments were employed. The IR spectrum assignment of paracetamol and its metal complexes are presented in Table 1. The structure determination of the complex was carried out based on the comparison of the spectrum of free paracetamol with the spectrum of its metal complex.

It was observed that absorption bands at 3325.28 cm and 3163.26 in the paracetamol IR spectrum were assigned to O-H and N-H groups, respectively. In case of N-H groups, this band underwent a zero intensity at the complex spectrum, providing proof that this group is one of the coordination positions of paracetamol.

The strong band at 3325.28 in paracetamol shown for OH band was observed in a different manner. This band was also appeared in the complex spectrum but experienced a shift in intensity to 3227.06 cm^{-1}. This phenomenon explains that this functional group located on the paracetamol molecule is connected to the metal ion without losing a hydrogen atom, giving evidence that this unit is another coordination site on the paracetamol. In addition, the strong absorption bands at 1625 cm- in the paracetamol spectrum was attributed to C=O group stretching. The complex spectrum showed a band absorption shift noted at this site, ranging 1508-1650, indicating a coordination site through this group.

Band at 1324 cm in the complex was contributed to C-N vibration. These band absorption assignments are summarized in Table 1, and the IR spectra of paracetamol and its complexes are shown in Figures 1 and 2.

Table 1: Selected IR spectral assignment of paracetamol (par) and its metal complex

Active group	*Paracetamol*	*Complex*	*Range*
OH H.bended	3325.28	3227.06	3000–3600
NH secondary stretch	3163.26	—	3100–3600
C = O	1650.36	1508-1630	1640–1720
CH3 bend	1508.33	1508.33	1371–1450
C – O	1236.37	1236.37	1000–1300
C – N	1371.39	1371.39	1000–1350
C = C aromatic	1608.63	1608.63	1475–1600

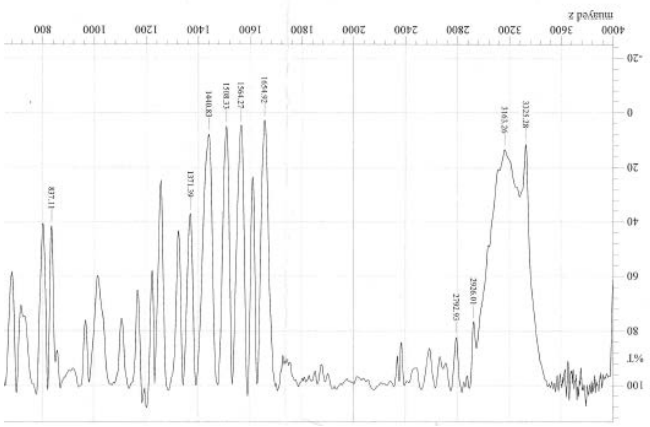

Figure 1: FTIR spectrum of free paracetamol.

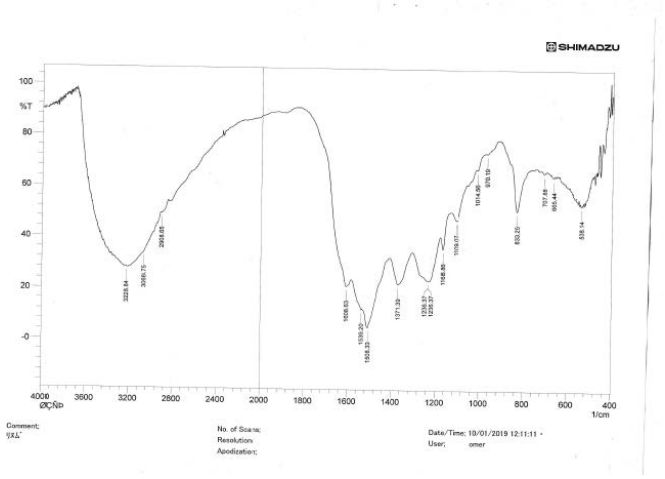

Figure 2: FTIR spectrum of Al(III)- paracetamol complex.

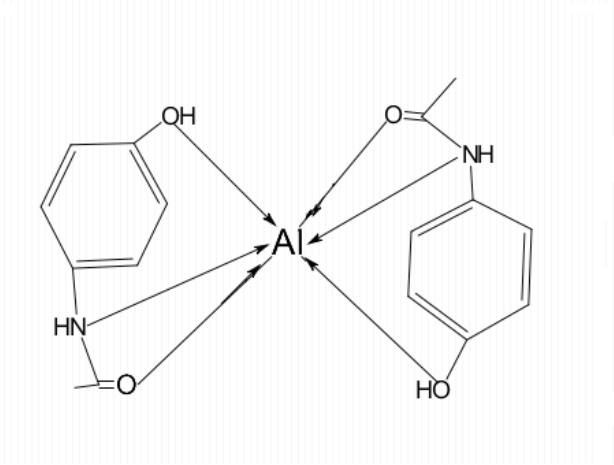

Figure 3: A proposed structure of Al(III) complex

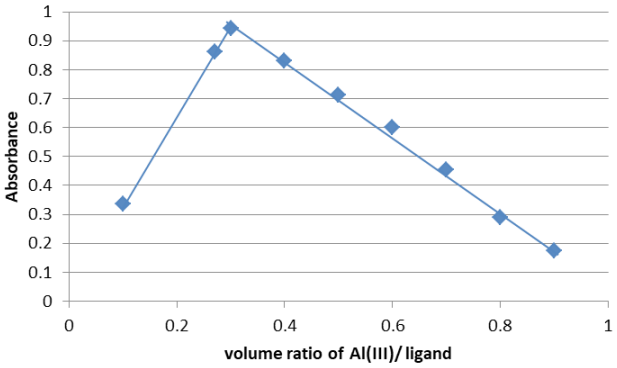

Figure 4: Job's plot for A(III)-paracetamol complex. The volume fraction of reagents where two straight lines meet is 0.32. The mole ratio is 0.32:0.68 which corresponds to 1:2 metal-ligand stoichiometry.

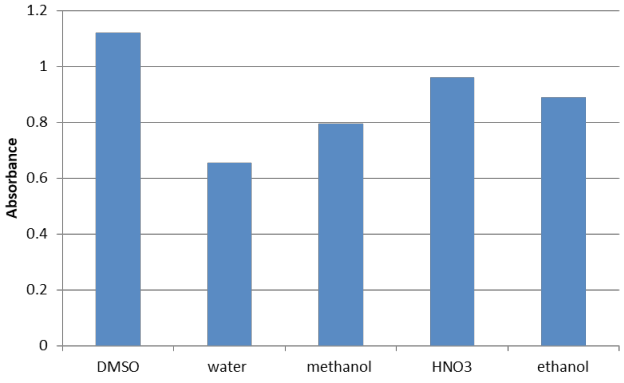

Fig. 5: Effect of solvent on the absorbance of Al(III)-paracetamol.

The Electronic Absorption Spectrum of Paracetamol Complex

The formation of Al(III) complex of paracetamol was also studied by UV–Vis spectrophotometer, where the Electronic absorption spectra of free paracetamol and its complex recorded in DMSO in the 200-700 nm. It was observed that the UV spectrum of free paracetamol had an absorption band at a different wavelength than that of its complex. The free paracetamol was measured at 300 nm, while the complex was recorded at 327 nm, indicating the newly formed complex could have n π^* electronic transition. This transition phenomenon was found in some metal complexes with paracetamol.

Based on the collected data above, it was found that the complex have octahedral geometry. Thus The complex's structure can be suggested as shown in Figure 3.

The effect of solvents such as methanol, ethanol, dimethylsulphoxide (DMSO), Nitric acid and distilled water was investigated at 1.5 mg/L

The absorbance of Al(III)-para complex varied depending on the solvent used. The reaction mixture was partially soluble in methanol, and distilled water. The absorbance for Al(III)-para complex in other solvents is shown in Figure 4. It is noticeable from the Figure that the highest absorbance was obtained in DMSO. Therefore, DMSO was the best solvent for the Al(III)-para solubility at room temperature.

Result of Stoichiometry by Job's Method of Continuous

Variation Jobs is presented in Figure 5. The absorbance of each mixture is measured and plotted against the mole fraction. The plot measurements result in 1:2 metal-ligand stoichiometry.

CONCLUSION

This work investigated the preparation of and characterization of paracetamol- aluminum complex. Traditionally, the literature in this research area has focused on the study of complexes of paracetamol with transition metals or alkaline earth metals. Nevertheless, the highlight of this study was

the successful synthesis of the complex of paracetamol with aluminum. To our knowledge, this is the first compound containing aluminum ion as central metal with acetaminophen. The compound Al(para)2 Cl_3 was produced from mixing an alcoholic solution of paracetamol with an aqueous solution of AlCl3 with proper molar ratios. This research used Infrared spectroscopy and UV-spectrophotometric method to elucidate the tentative structure of the synthesized complex. These techniques revealed that paracetamol behaves as tribentate ligand towards the metal ion. The attachment of the ligand to the central metal was via the hydroxyl, amine, and carbonyl groups, two molecules of which is bounded to the metal ion.

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