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Synthesis of New Silver Analgesic Drug.

Omar B Ibrahim[1], Eman M Elsewedy[2], Mohamed Y El-Sayed[3], Abdel Majid A. Adam[1] and Moamen S Refat[1,4]*.

[1]Department of Chemistry, Faculty of Science, Taif University, Al-Hawiah, Taif, P.O. Box 888 Zip Code 21974, Saudi Arabia
[2] Department of Chemistry, Huraymila College of Science and Humanities, Shaqra University, Saudi Arabia
[3]Department of Chemistry, Faculty of Science, Zagazig University, Zagazig, Egypt
[4]Department of Chemistry, Faculty of Science, Port Said University, Port Said, Egypt

ABSTRACT

Enhance the efficiency of the drug in the presence of silver metal ions by formation of new complex. This complex was proven using spectroscopic and thermal analysis. the infrared spectral assignments, the silver(I) ions coordinated to para drug through two place of coordination (deprotonated of –OH) and (deprotonated of –NH and oxygen of carbonyl) the molar conductivity silver(I) complex is non-electrolytes. Antibacterial and antifungal activities of silver(I) paracetamol complex are assessed against Escherichia coli (G –ve), Bacillus subtilis (G +ve) and antifungal (Aspergillus niger and Aspergillus flavus). The antimicrobial activity of Ag(I) complex is found to has high activity against bacteria and fungi.

Keywords: Paracetamol, Silver(I) complex, antimicrobial test, spectroscopic studies.

Corresponding author

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INTRODUCTION

The paracetamol (Fig. 1) is one of the famous analgesic drugs which is commonly named as N-acetyl-4-amino-phenol. Paracetamol has an antipyretic medication with little toxicological side effect [1-7]. The fluorometry [8], luminescence [9], electrochemical [10], nuclear magnetic resonance, mass spectroscopy [11] and liquid chromatography [12] are different analyses techniques used to determination of paracetamol drug in pure and pharmaceutical fashions. Paracetamol has a side effect as hepatotoxic in man and animals if it was taken with over dose [13-17]. Herein in this research paper, we aimed to enhance the efficiency of the drug in the presence of silver metal ions by formation of new complex. This complex was proven using spectroscopic and thermo gravimetric analyses.

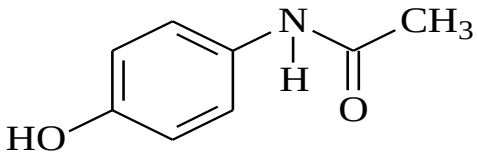

Fig 1: Chemical structure paracetamol

EXPERIMENTAL

Materials

Reagents (paracetamol and silver(I) nitrate) are in analytical grade and used without further purification.

Instrumentations

The elemental analysis (%carbon, %hydrogen and %nitrogen) results were measured using CHN-2400 Perkin Elmer analyzer instrument. FT-IR spectra were scanned on Bruker FT-IR spectrophotometer within 4000-400 cm^{-1} region. The UV-vis. spectra of reactants and silver(I) complex were scanned using Perkin-Elmer Lambda 4B spectrophotometer in dimethyl sulphoxide solvent. The thermo gravimetric analyses TG/DTG were carried out in nitrogen atmosphere using Schimadzu TGA-50H thermal analyzer.

Synthesis

The 1 mmol of $AgNO_3$ was dissolved in 20 mL distilled water and then mixed to 20 mL of methanolic solution of paracetamol with 1 mmol ratio under magnetic stirring. The pH of mixture was neutralized at 7-8 using diluted ammonium hydroxide solution. The mixture was refluxed at 60 °C and left to evaporate slowly at room temperature. The precipitate was filtered off, washy with hot methanol and dried at 60 °C.

Microbiological investigation

The biological activity of silver(I) complex was tested against bacteria and fungi with more than one test organism. The organisms used in the present investigation including two bacteria (B.subtilis Gram +ve), (E. coli Gram –ve) and two fungi (Aspergillus niger and Aspergillus flarus). The results of microbiological investigations of bacterial and fungi against synthesized silver(I) complex were assessments.

RESULTS AND DISCUSSION

Elemental analyses

The experimental data of %carbon, %hydrogen and %nitrogen are matched with the calculated values (Table 1). The elemental analyses results are support that NO_3^- ions not detected. The silver(I) complex is air stable with highly melting point > 300 °C.

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Table 1: Elemental analyses and physical results of Ag(I) complex

[Ag_2(para)]	M.wt (g/mol)	%C		%H		%N		%M		Λ (Ω^{-1}. $cm^2.mol^{-1}$)
		Found	Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.	
	364.88	27.0	26.33	1.87	1.93	4.00	3.84	58.50	59.12	7.0

Molar conductivity

The molar conductance value of the silver(I) complex of paracetamol drug in DMSO solvent with concentration of $1.00x10^{-3}$ M was found to be 7.00 Λ (Ω^{-1}. $cm^2.mol^{-1}$) at 25 °C. This data suggested that silver(I) complex is non-electrolytes.

Infrared spectra

The infrared assignments data of paracetamol free drug and its silver(I) complex are tabulated in Table 2 and silver(I) complex is shown in Fig. 2. Based on the comparison between the infrared spectra of free paracetamol drug ligand and its silver(I) complex, it has been discussed that, the absorption band at 3300 cm^{-1} and 3200 cm^{-1} of free paracetamol have been assigned to –OH and –NH stretching vibration motions. These bands have been absence in the spectra of the silver(I) complex due to the involvement in complexation. The strong-to-medium absorption bands at 1650 and 1260 cm^{-1} in the spectrum of para drug are assigned to the stretching vibration bands of ν(C=O) and ν(C-O), respectively. These bands are shifted to lower wavenumbers at 1627 and 1100 cm^{-1} due to sharing in coordination mode. The presence of new absorption band at 510 cm^{-1} in silver(I) complex is assigned to ν(Ag -O) stretching vibration. Upon the infrared spectral assignments, the silver(I) ions coordinated to para drug through two place of coordination (deprotonated of –OH) and (deprotonated of –NH and oxygen of carbonyl group) as shown in Fig. 3.

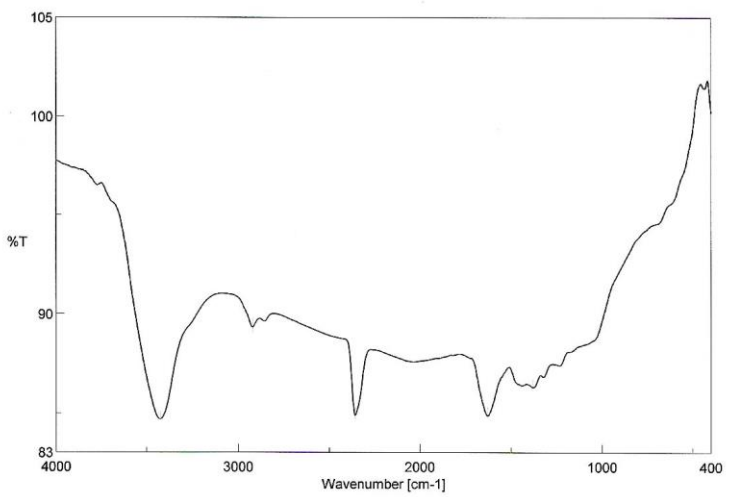

Fig 2: FT-IR spectrum of Ag(I) complex.

Table 2: Infrared frequencies within 4000-400 cm^{-1} of para and its Ag(I) complex

Compound	ν(OH) + ν(NH)	ν(C=O)	δ(CNH) amide group	ν(C-O) phenyl group	ν(M-O)
para	3300, 3200	1650	1560	1260	-
[Ag_2(para)]	-	1627	1550	1100	510

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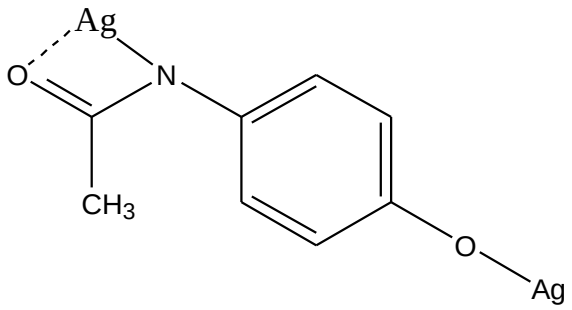

Fig 3: Suggested structure of Ag(I) complex.

UV-vis. Spectra

The formation of the Ag(I) complex was also confirmed by UV-vis. spectra in DMSO solvent within the 200-600 nm range. It can see that free para has two absorption bands at 300 and 390 nm due to π-π* intra-ligand transition of the aromatic ring and n-π* electronic transition, respectively.

Thermo gravimetric analyses

The heating rate was controlled at 10°C/min under nitrogen environment. The weight loss was scanned from room temperature till 1000 °C. The thermo gravimetric curve of silver(I) complex is shown in Fig. 4. The thermal decomposition of [Ag_2(para)] complex exhibit at two step. These steps are occurring at 200-1000 °C and corresponding to the decomposition of para molecule with a weight loss of 11.4%. The final residual product is silver metal contaminated with few carbon atoms.

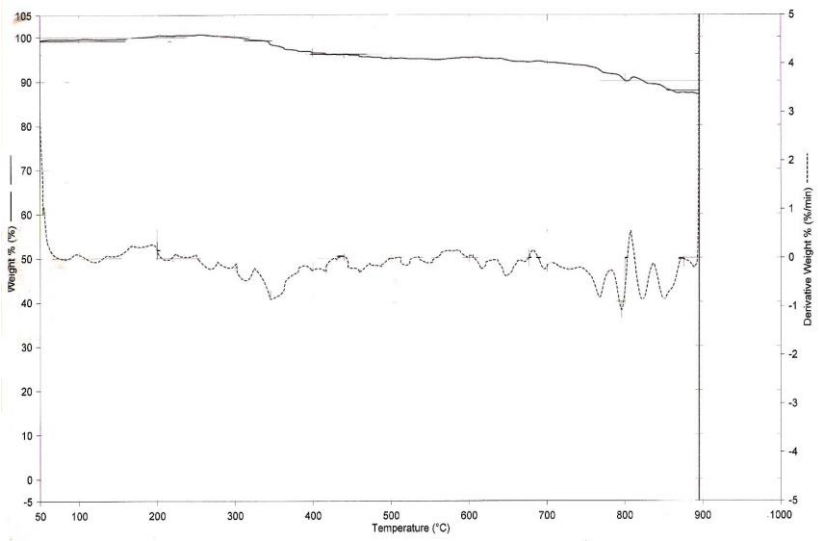

Fig 3: TG/DTG curve of Ag(I) complex of paracetamol

Microbiological investigation

Antibacterial and antifungal activities of silver(I) paracetamol complex are assessed against Escherichia coli (G –ve), Bacillus subtilis (G +ve) and antifungal (Aspergillus niger and Aspergillus flavus). The antimicrobial activity scanned based on the size of inhibition zone. Ag(I) complex is found to has high activity against bacteria and fungi. The data listed in Table 3 and is shown in Fig. 4.

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Table 3: Antimicrobial data of para complex

Sample	Bacillus subtilis	E. coli	Aspergillus niger	Aspergillus flavus
Control	0	0	0	0
Ag(I) complex	1.4	1.1	1.8	2.1

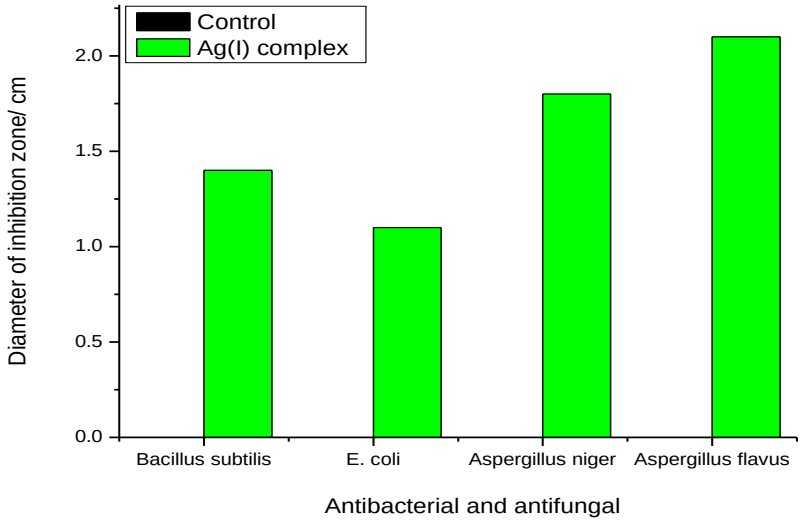

Fig 4: Statistical data of biological activities of DMSO control and silver(I) complex

CONCLUSION

Solid complex has been prepared and characterized. Para drug react with Ag(I) by molar ratio (1:2) . The spectral data indicate the para drug co-ordinate from two places via deprotonated (-OH& -NH) and oxygen of carbonyl. Ag para complex is thermally stable and has high biological activity. This work is very industrial and biological important. The metal drug complex has significant effect on therapeutic action of the drugs.

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