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Research Article

Inhibition Effect of Gold (III) Theophylline Nano-complex on ALT Enzyme Activity in Human Serum of Iraqi Patients with Liver Disease

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I N F O

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A B S T R A C T

Introduction: The ultrasonic sonication approach was used to create an Au(III) nano complex with theophylline.

Methods: To explore and suggest the structure of the nano complex, UV-Vis spectroscopy, Fourier transform infrared (FT-IR), and carbon hydrogen and nitrogen (CHN) elemental studies were used. The FE-SEM was used to prove the nanoscale of the prepared complex and was to be less than 20 nm. The effect of the gold nano complex (Au $(THP)_2$ $(Cl)_2$) on alanine transaminase (ALT) activity in the serum of chronic liver disease patients was investigated.

Results: Compared to the control group, the patients with chronic liver disease with and without nano complex had a significant rise in serum levels of ALT activity ($P < 0.001$). Furthermore, in individuals with chronic liver disease who received nano complex, the blood levels of ALT activity were significantly lower than those who did not receive nano complex. The reason is that the Au nano complex aggressively interacts with carboxylic groups of important enzymes and inactivates them; further, the Au nano complex had an inhibitory effect on serum ALT activity.

Keywords: Liver Disease, Nano Complexes, Serum Alanine Transaminase

Introduction

Nanotechnology is one of the most promising technologies for imparting cutting-edge features in many scientific areas.[1-3] Nanomaterials have recently received much attention due to their applications in biomedical, physiochemical, drug transport, sensing, imaging, and chemotherapy.[4-6] TMCs (transition metal complexes) are a fascinating class of molecules that can be employed in practically any discipline of chemistry.[7, 8] TMCs are an important part of the human body's structural and functional aspects, and they play a key role in a variety of physiological and pathological processes.[9,10] According to studies,[10-14] nano complexes exhibit distinct physical, chemical, and biological properties. Gold (Au) is considered an important field of research because it has a surface Plasmon resonance

(SPR) and has a preference in clinical applications over other mineral particles in terms of biocompatibility and non-cytotoxicity,[15] as well as their application in cancer treatment and imaging, genetic disease diagnosis, and photothermal therapy.[16,17] Purines have also been widely explored in metal complexes.[18-22] These complexes play an important role in many biological interactions.[23,24] The study of transition metal complexes as medications for various human ailments has shown significant results. Transition metal complexes are the most widely used chemotherapeutic agents and contribute significantly to medical therapies.[25] Alanine transaminase (ALT), also known as glutamic pyruvic transaminase, is a carrier enzyme located in the liver.[26,27] The ALT function catalyses the reversible transamination process of an amino group into α- ketoglutarate, pyruvate, and L-glutamate.[28] This enzyme is used to diagnose liver disorders because it is more selective than aspartate transaminase (AST).[29] When liver damage occurs, ALT is released into the bloodstream and is increased in serum patients. As a result, the ALT is a useful tool for diagnosing liver lesions.[30] In this project, we prepared theophylline (THP) with Au ion as a nano complex to study the inhibition of the serum ALT activity for patients with chronic liver disease.

Experimental PART

Standard operating procedures (SOPs) have been followed in conducting the study protocols.

Materials

Sigma-Aldrich provided all of the chemicals and solvents that were used. In addition, deionised water was used throughout the research process.

Synthesis of Gold (III) Theophylline Nano Complex

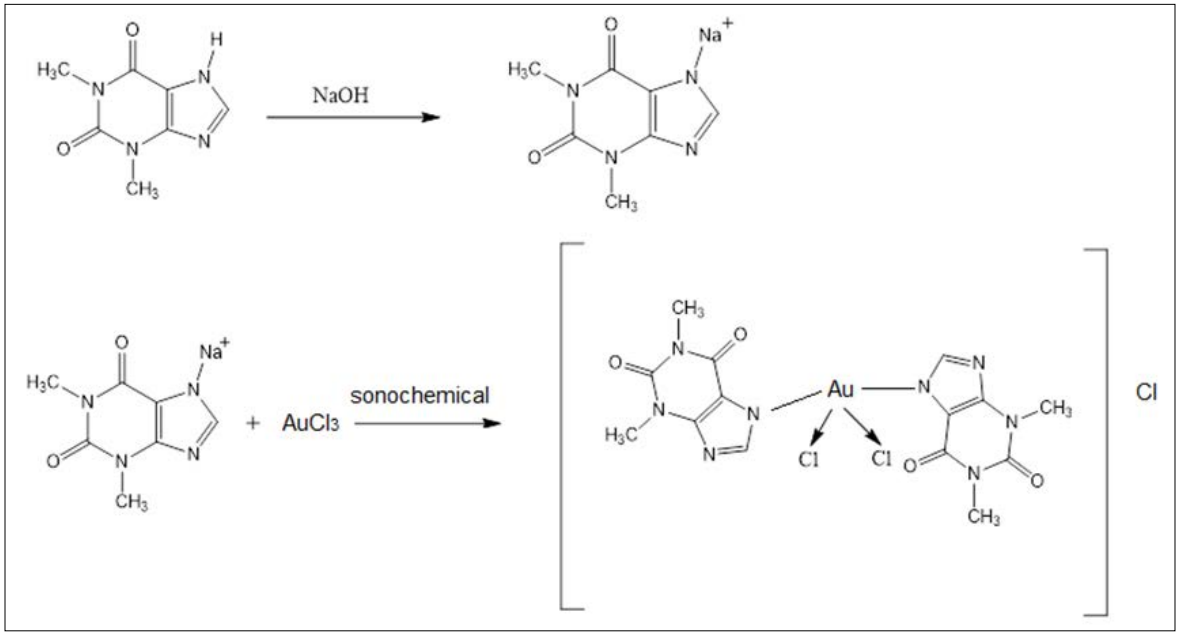
As shown in Scheme 1, a nano complex of Au (III) with theophylline (THP) as a ligand was produced utilising ultrasonic sonication. To make the sodium salt of the ligand, theophylline (0.006 mol) was dissolved in a 30 mL fresh NaOH (0.006 mol) solution. After heating the solution to 70°C, gold (III) chlorides (0.003 mol in 30 mL) were added to the aqueous solution. At 70°C, the solution combination was ultrasonic sonicated for 3 hours. Following that, crystals of good grade developed after overnight incubation at room temperature. Filtered novel complex was then rinsed and dried thoroughly in the air.

Complex (Au (THP)$_2$ (Cl)$_2$): color: yellow; Anal. Calc. for $C_{14}H_{14}N_8O_4AuCl_2$: C, 26.84; H, 2.24 N, 17.89; Au, 31.47. Found: C, 25.43; H, 2.11; N, 18.32; Au, 30.53%.

Specimen Collection

Before any procedure, each patient provided with written informed consent and approval for this study was obtained by the ethical committee of Al-Nisour University College.

The blood samples were taken at random from 35 patients in Baghdad, Iraq that had liver disease, independent of their age or gender, and 35 controls were included in the study. These samples were drawn with plastic disposable syringes and allowed to clot at room temperature for 30 minutes before centrifuged at 700 g for 15 minutes to separate the components. The serum was extracted from the clots and placed in disposable tubes right away. The automation analyser was used to determine the amount of ALT. The serum samples were extracted and immediately deposited in plastic tubes, then stored at (-20ºC) to study later.



Scheme 1.Gold (III) Nano Complex Synthesised

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Characterisation

Some devices characterised gold nano complex. The U.V-Vis spectrum, FT-IR spectra, FESEM and CHN Elemental analysis were used to investigate and suggest the structure of the Nano complex.

Statistical Analysis

The statistical study results were performed using one-way ANOVA and Microsoft Office (SPSS version 24). The results were presented as mean, standard deviation (SD), with a significance level of p = 0.01 regarded as highly significant.

Results and Discussion

FTIR Spectroscopy Analysis

Theophylline's FTIR spectrum Figure 1 revealed an absorption band at (3110 cm^{-1}) corresponding to v (NH), which vanished in the FTIR spectra of gold nano complex Figure 2. This revealed that the (NH) group was involved in the theophylline-gold ion coordination. At 560 - 575 cm^{-1}, a new band in the complex emerged, referring to metal coordination (N-Au). In addition, due to hydrogen interactions formed by water molecules with the carbonyl and amine groups, all vibration bands in the nano complex moved to a lower frequency than in free theophylline.[31]

UV Spectrophotometry Study

There were UV-visible absorption ranges of theophylline and its gold Nano complex (III) between 200 and 800 nm in hot water. Theophylline's UV-visible spectrum has three UV-region bands. At 276 nm, the first band can be attributed to the transition from π → π*. At 296 and 305 nm, the second and third bands are assigned to a single pair's oxygen and nitrogen electrodes as shown in Figure 3. These transitions are moved to higher values in the electronic spectrum of the nano-complex. Therefore, the compound has three 513, 349 and 311 nm absorption ranges attributed to $^1A_1g \rightarrow {}^1A_2g$, $^1A_1g \rightarrow {}^1B_1g$ and $^1A_1g \rightarrow {}^1Eg$ transitions. The placements of these bands correspond to the low-spin square square-planar geometry.[32]

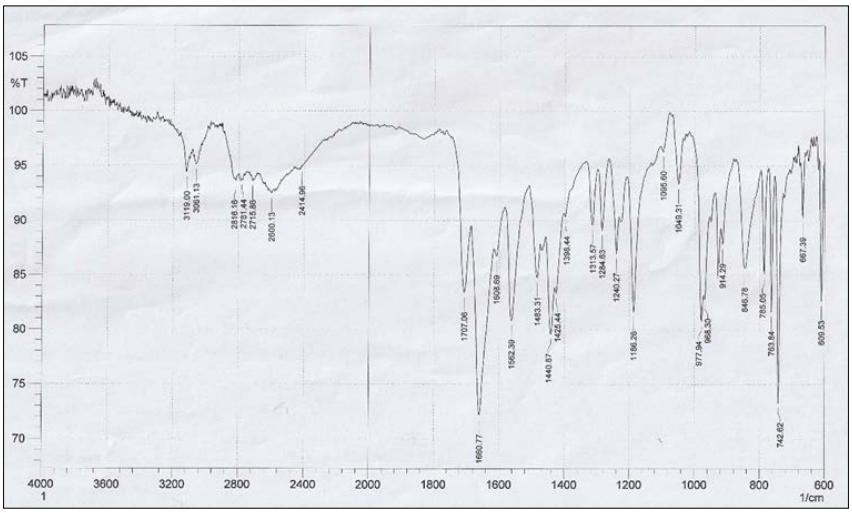

Figure 1.FTIR Spectrum of Theophylline (THP)

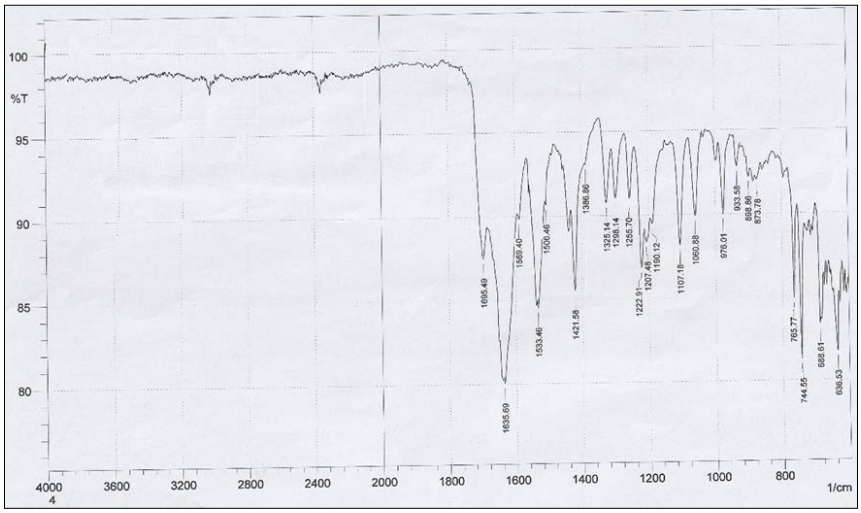

Figure 2.FTIR Spectrum of the [Au $(THP)_2$ $(Cl)_2$] Nano Complex

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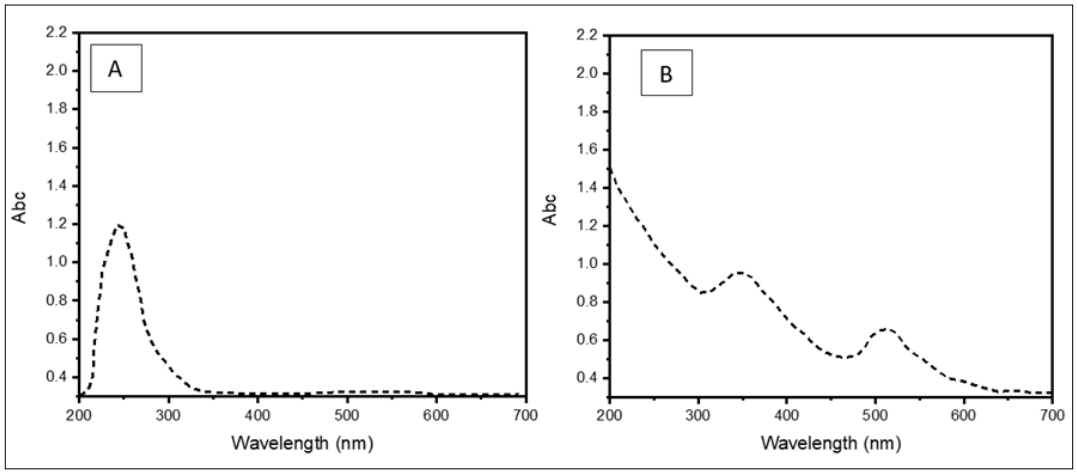

Figure 3.UV-Vis Spectra of A) Free Theophylline and B) [Au $(THP)_2$ $(Cl)_2$] Nano Complex

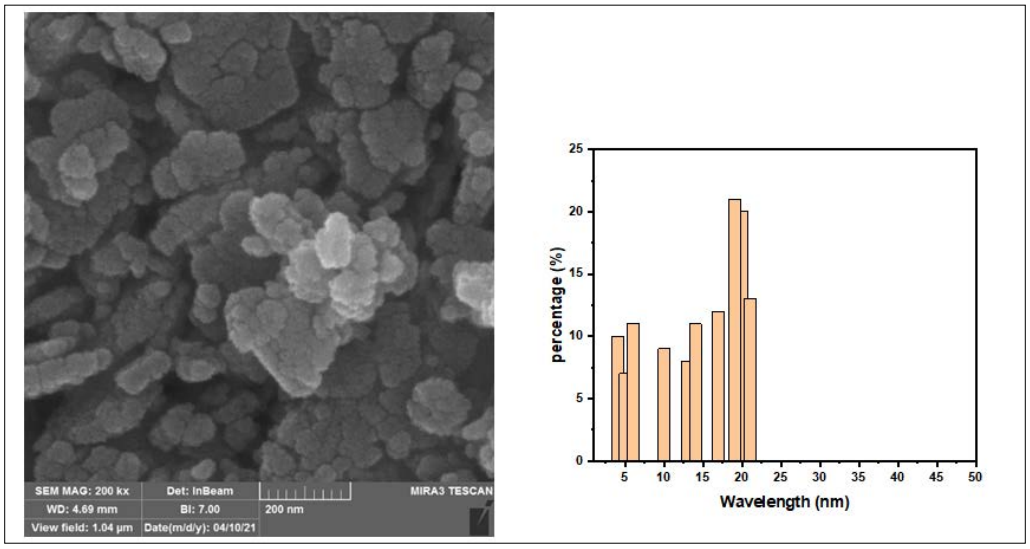

Figure 4.FESEM of (Au $(THP)_2$ $(Cl)_2$) Nano Complex

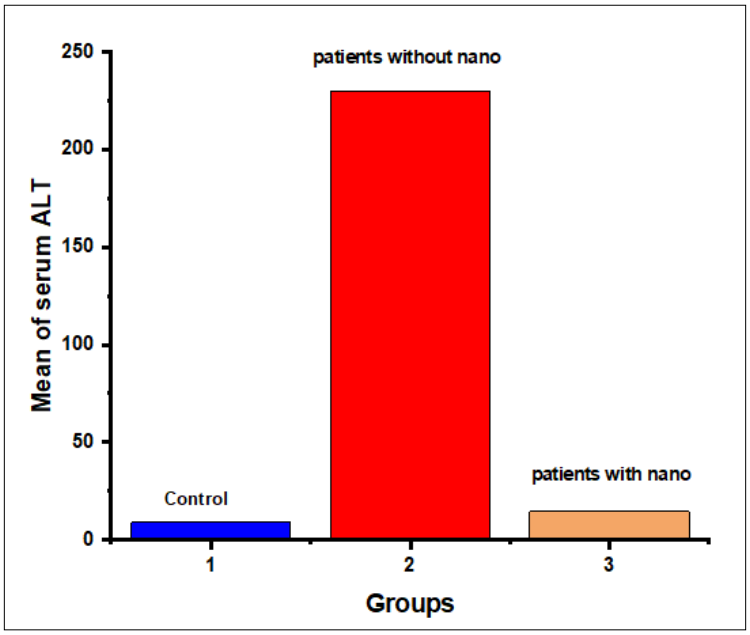

Figure 5.ALT Level of Controls and Chronic Liver Disease

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FESEM Study

FESEM was used to analyse the surface morphology of the sample. The microscopy examination revealed that the synthesised complex was not in direct contact with the aggregates, indicating that the complex had stabilised. The majority of the synthesised Au nano complexes had spherical and irregular forms. The morphological shapes and sizes of the aggregations were defined using fractal dimensions and the box-counting approach.[33] A representative FESEM micrograph revealed a particle size range of 10–20 nm (Figure 4).

Effect of [Au $(THP)_2$ $(Cl)_2$] Nano Complex on Alanine Transaminase (ALT) Enzyme Activity

Table 1 shows the effect of gold nano complex on ALT enzyme activity in human serum of patients with chronic liver disease in the current investigation. According to the results of the automated analyser, there was a highly significant increase in serum levels of ALT activity in patients with chronic liver disease with and without nano complex as compared to the control group ($P < 0.001$). In individuals with chronic liver disease who received nano complex, blood levels of ALT activity were significantly lower than those who did not receive nano complex. This is due to the nano complexes' interaction with the enzyme's carboxylic group, which results in inhibition as shown in Figure 5.

Table 1.Alanine Transaminase Level in Sera of Controls and Chronic Liver Patients

Groups	Alanine transaminase (Mean ± SD)	p-value
Control	8.85 ± 2.42	p < 0.001
Patients without nano complex	230 ± 27.4	p < 0.001
Patients with nano complex	14.5 ± 3.46	p < 0.001

P < 0.001 = highly significant.

The results are of high importance in individuals with chronic liver disease who received nano complex this attribute to Au nano complex had an inhibitory effect on serum ALT activity and so minimising liver cell damage and might be used as a cell protectant agent but need more research on cell toxicity.

Conclusion

Complexes in nanoscale were synthesised using the ultrasonic sonication approach. Therefore, the nano complex may be easily manufactured without aggregation using our approach. The current study is the first to describe how the gold nano complex affects Alanine transaminase (ALT) activity in serum from Iraqi chronic liver disease patients. The results revealed that (Au $(THP)_2$ $(Cl)_2$) in nanoscale had a significant inhibitory effect on enzyme activity.

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Conflict of Interest: None

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