



Original Article

Antibacterial Activity of Copper (II) Complexes of Maleic Acid: Thermal Studies, and New Precursors for Preparation of CuO

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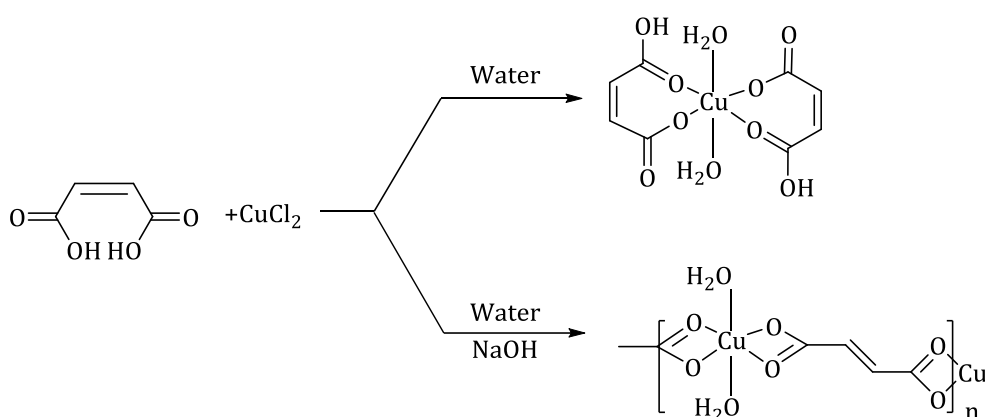
CuO nanoparticles

Antibacterial activity

ABSTRACT

In this paper, two copper(II) complexes based on maleic acid ligand, namely $[\text{Cu}(\text{MA})_2(\text{H}_2\text{O})_2]$ (**1**) and $[-\{(\text{H}_2\text{O})_4\text{Cu}_2\}(\mu\text{-MA})\}_n]$ (**2**) have been synthesized from the reaction of CuCl_2 and maleic acid in aqueous solution and characterized by CHN, FT-IR, XRD and TGA. In addition, from the calcination of these complexes at $600\text{ }^\circ\text{C}$ for 3 h in air atmosphere, CuO particles were prepared and characterized by FT-IR, XRD and SEM. Furthermore, antibacterial activity of them were tested against two Gram-positive (*S. aureus* and *B. cereus*) and two Gram-negative (*E. coli* and *P. aeruginosa*) strains. Results shows that the complexes **1** and **2** exhibit enhanced antibacterial activity than CuO particles.

GRAPHICAL ABSTRACT



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Introduction

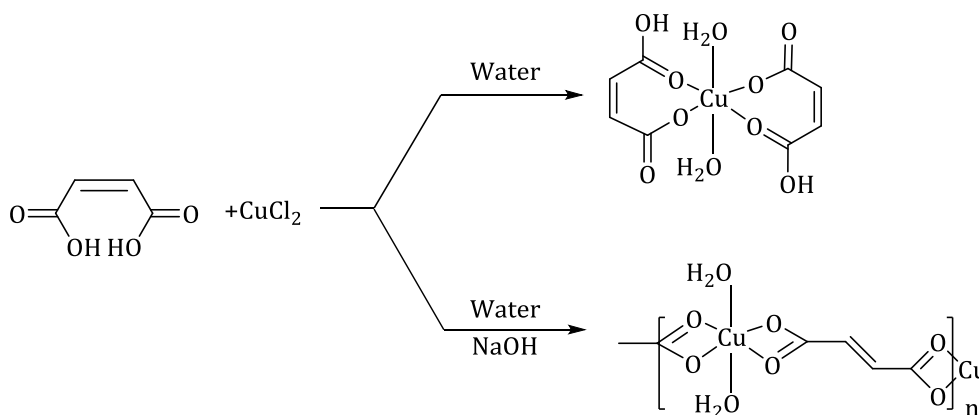
In recent years, transition metal complexes have received substantial attention due to their various applications [1-3], and also play an important role as antibacterial agents in biological process [4-8]. Antibacterial agents divide into two categories, organic and inorganic compounds [9]. Organic compounds are flexible and have strong and efficient antibacterial activities but the short life of them limit the antibacterial application of them [9]. Inorganic compounds have high thermal and chemical stability and show good antibacterial activities [4-13]. Ye et al. [9] prepared MOFs of [Zn(format)₂(4,4'-bipy)] as superior antibacterial activities. Gomathi et al. [10] synthesized Co(II) and Ni(II) complexes which possessed high antibacterial activity at low concentration. Angelusiu et al. [11] have reported superior antibacterial activities of Cu(II), Co(II) and Ni(II) arylhydrazone ligands. Liu et al. [12] synthesized novel Cu(II) and Zn(II) Schiff base complexes and reported the antibacterial activity of them. Recently, efforts to prepare metal complexes have attractive aspects due to their good antibacterial properties [5,9-13]. Often, complexes show better antibacterial properties than ligands and free ions [9-13]. In recent years,

the interest towards the CuO nanoparticles has increased because of their application and activities such as optical property, antibacterial activity, catalytic reduction of 4-nitrophenol and photocatalytic removal of dyes from aqueous solution [14-20].

In this paper, we have reported preparation and characterization of two copper(II) complexes, [Cu(MA)₂(H₂O)₂] (**1**) and [Cu₂(MA)₂(H₂O)₂]_n (**2**), where MA is maleic acid (Scheme 1). In addition, CuO particles were prepared by solid-state thermal decomposition of **1** and **2** as new precursors.

Material and methods

All compounds such as CuCl₂·6H₂O, maleic acid, NaOH were purchased from Merck and Aldrich and used without further purification. Elemental analyses were carried out using a Heraeus CHN-O-Rapid analyzer. FT-IR spectra were recorded using Perkin-Elmer FT-IR spectrophotometer. The Perkin-Elmer TGA analyzer was used for the thermogravimetry analysis in air atmosphere (25-700 °C). XRD and SEM were recorded using Bruker AXS-D8 X-ray diffractometer (2θ=10-80°), and the TESCAN Vega Model scanning electron microscope, respectively.



Scheme 1: Procedure and chemical structure of copper(II) complexes **1** and **2**

Preparation of copper complex 1

Maleic acid (0.2 mmol) in 5 mL deionized water was added to a solution of CuCl₂·6H₂O (0.1 mmol) in deionized water (5 mL). The mixture was stirred at 25 °C for 60 min. Greenish-blue precipitates were filtered, washed by cold methanol and dried for several days. *Anal. Calcd.* for C₈H₁₀O₁₀Cu: C, 29.13%; H, 3.03%. Found; C,

29.19%; H, 3.06%. FT-IR (KBr, cm⁻¹): 2997-3500 (O-H and C-H), 1725, 1606 (C=O), 1431, 1269, 1200, 1094, 1042, 937. 659, 581, 473.

Preparation of copper complex 2

A solution of maleic acid (0.2 mmol) in deionized water (5 mL) was added to a stirred solution of CuCl₂·6H₂O (0.1 mmol) in deionized water (5

mL). A solution of NaOH (0.1 M) was then added dropwise with constant stirring. The mixture was stirred at 25 °C for 60 min. Blue precipitates were filtered, washed by cold methanol and dried for several days. *Anal. Calcd.* for $C_4H_6O_6Cu$: C, 22.48%; H, 2.81%. Found; C, 22.39%; H, 2.84%. FT-IR (KBr, cm^{-1}): 3454 (O-H), 1628, 1601 (C=O), 1396, 1202, 1094, 1043, 982, 896, 850, 684, 603.

Preparation of CuO particles

To prepare CuO particles, the obtained complexes were calcinated at 600 °C for 1.5 h (complex **1**) and 3 h (complex **2**). The CuO particles were characterized by FT-IR, XRD and SEM.

Antibacterial studies

The antibacterial properties were tested against different pathogenic bacteria such as *E. coli*, *P. aeruginosa*, *S. aureus* and *B. cereus* [21-23]. To estimate the antibacterial activity of the compounds, good diffusion assay was performed. Nutrient agar was poured onto the Petri dishes and bacteria were spread on the plate uniformly. Then the aqueous solutions of compounds (0.01 g in 1 mL de-ionized water) were gently placed over the agar gel and finally the plates were incubated for 24 h at 37 °C.

Result and Dissection

Synthesis and characterization

Complex **1** has been prepared by the reaction of $CuCl_2$ and maleic acid in an aqueous solution and complex **2** has been prepared in an alkaline aqueous solution. In the FT-IR spectra of **1** and **2** (Figure 1), there are several peaks assigned to the C-H, O-H, C=O and other stretching modes. A sharp peaks at about 1725, 1606 and 1431 cm^{-1} assigned to the C=O and C-C stretching in complex **1**, while these peaks appeared at 1628, 1601, and 1396 cm^{-1} in complex **2** [24]. The appearance of the carbonyl group peak in the lower wave numbers (1628 cm^{-1}) in complex **2** confirmed that the maleic acid coordinated to copper(II) ions as anionic bidentate ligand. Also, the lower solubility of complex **2** than **1**, predicts that this complex is polymer and maleic acid acts as bridge ligand (Scheme 1). Complex **1** showed a multiple weakly peaks at about 3200-3500 cm^{-1} that correspondence to O-H vibration of OH and water molecules coordinated to copper(II) ion. In complex **2**, a sharp and broad peak at 3455 cm^{-1} assigned to the vibration of water molecule coordinated to copper(II) ion.

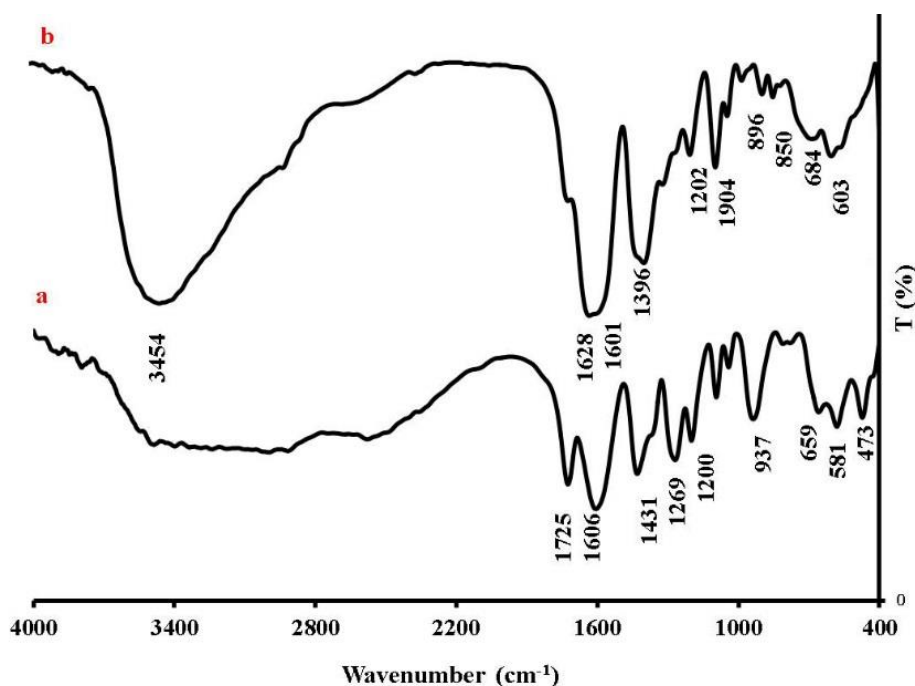


Figure 1: FT-IR spectra of a) complex **1** and b) complex **2**

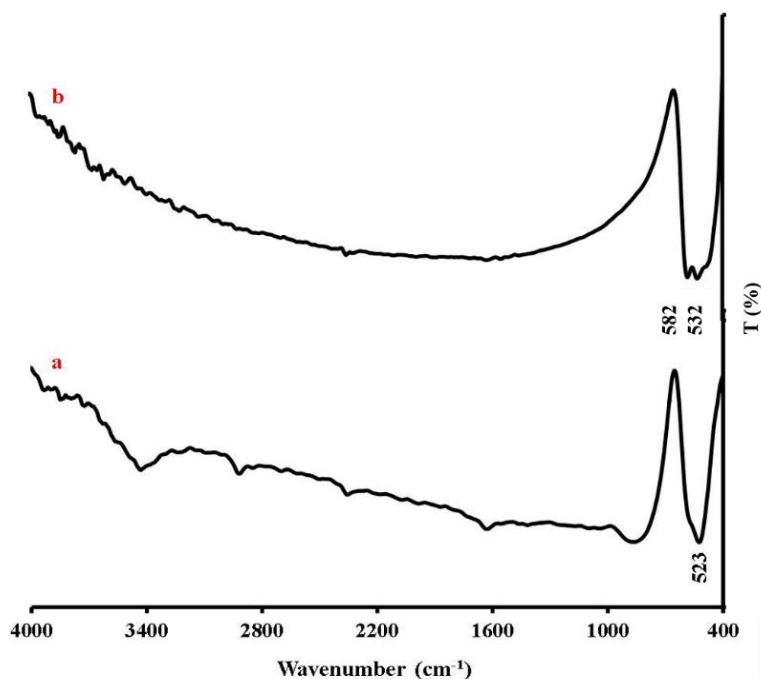


Figure 2: FT-IR spectra of CuO particles prepared from a) complex **1** and b) complex **2**

After calcination of complexes at 600 °C, vibrations related to organic bonds are expected to be eliminated and have only the vibration related to the oxygen metal ion. In the FT-IR spectra of the as-prepared CuO particles (Figure 2), there is one peak at 523 cm⁻¹ in the FT-IR spectra of the CuO particles prepared from **1**, while there are two peaks at 582 and 532 cm⁻¹ in the FT-IR spectra of the CuO nanoparticles prepared from **2**, assigned to the stretching vibration of Cu^{II}-O bond in monoclinic CuO nanoparticles [14, 23-27]. Copper(II) oxide has three structures such as monoclinic, tetragonal, and cubic phases. Among them, the monoclinic phase is the most symmetrical both structurally and electronically [28,29].

XRD patterns

XRD is a useful technique that helps us to determine the crystal structure or amorphous composition of the compounds. Due to the fact that each combination has its own diffraction pattern, it is easy to identify the type and structure of the desired combination from the diffraction pattern of each combination and comparison with standard diffraction patterns. Therefore, in order to identify the prepared compounds, their diffraction patterns have been prepared, and showed in Figures 3 and 4, respectively.

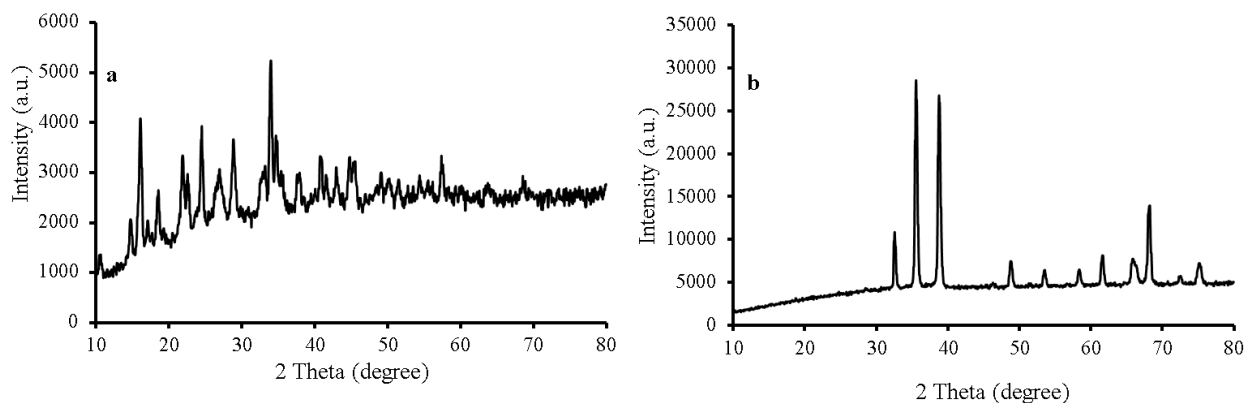
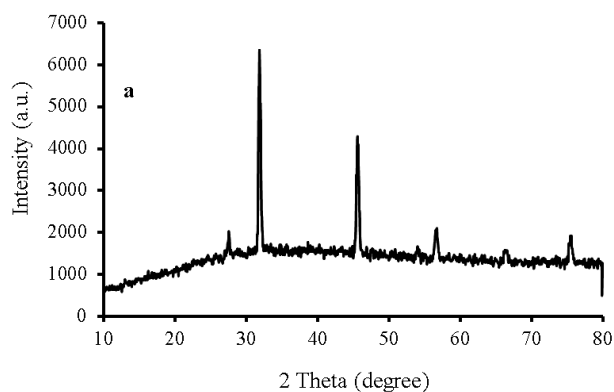


Figure 3: XRD pattern of a) complex **1** and b) its prepared CuO nanoparticles

In Figure 3a, there are various peaks at different 2θ . All of the peaks are sharp and broad and confirm that the prepared particles of the complex are small. After decomposition of the complex at 600 °C and removal of the organic groups of the complex, only metal oxide remains. The XRD pattern of the final product after decomposition at 600 °C is shown in Figures 3b and 4b. These XRD patterns confirmed the formation of copper oxide (CuO) particles. In these patterns, sharp and relatively wide peaks can be seen at different angles, $\approx 32.6, 35.6, 38.8, 48.7, 53.6, 61.7, 66.3, 68.2, 72.8, 74.9$, which



correspond to the standard pattern of the orthorhombic copper(II) oxide (JCPDS card no. 801268) [20,30]. XRD pattern of complex **2** (Figure 4a) is different from **1**, and there are 7 sharp and broad peaks at $2\theta = 27.5, 31.8, 45.9, 56.8, 66.5, \text{ and } 75.4$, due to the good crystallinity and different structure of **2** than **1**. However, the XRD pattern of the CuO nanoparticles prepared by decomposition of **2** (Figure 4b) is a little similar to that of CuO nanoparticles prepared from **1** [20-27,30].

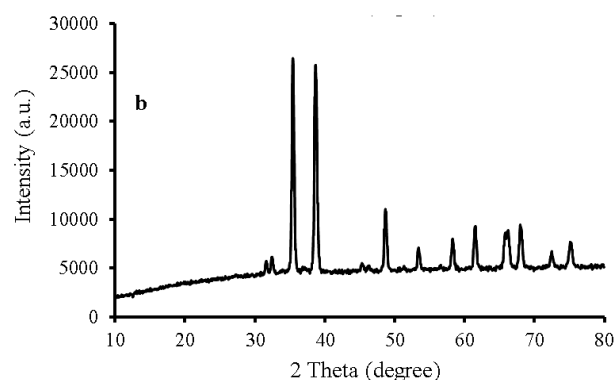


Figure 4: XRD pattern of a) complex **2** and b) its prepared CuO nanoparticles

SEM images

SEM technique is used to study the morphology of the compounds. SEM images of the complexes **1** and **2** and its CuO nanoparticles are shown in Figures 5 and 6, respectively. SEM Images of the complexes show that they are of irregular size and to some extent large crystalline compounds are also observed in them. While the size of the

prepared copper oxide nanoparticles is in a relatively narrow range. CuO particles prepared from complex **1** was agglomerated, while the CuO particles prepared from complex **2** was not agglomerated. As seen in SEM images, complexes **1** and **2**, have not the same shapes, while their CuO particles have similar shapes.

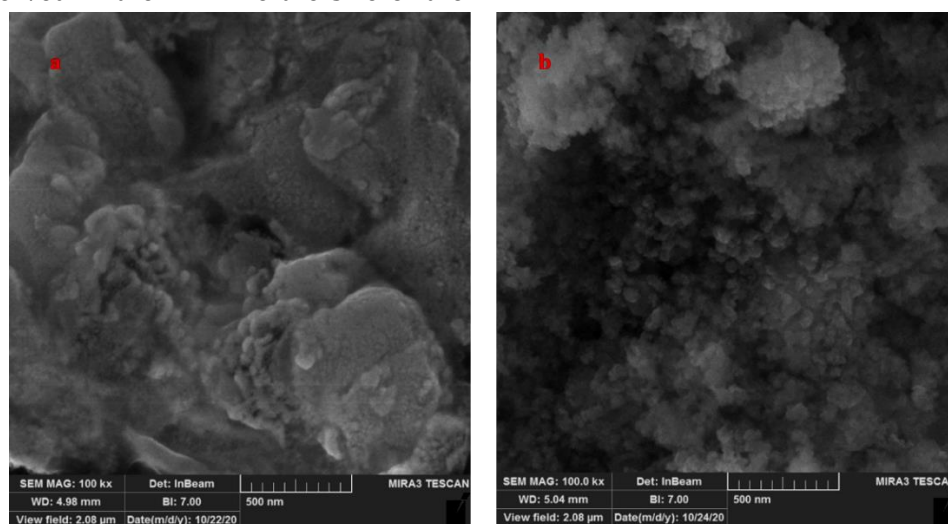


Figure 5: SEM images of a) complex **1** and b) as-prepared CuO particles

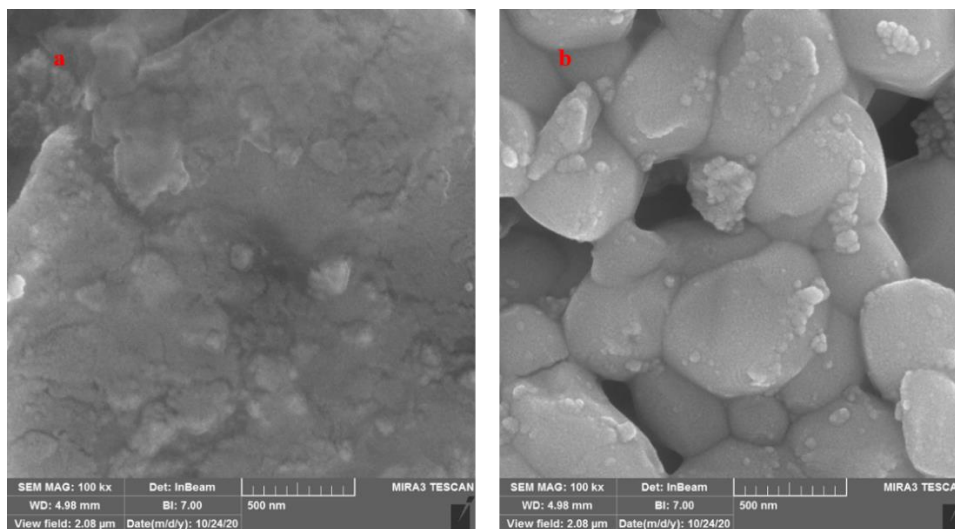


Figure 6: SEM images of a) complex **2** and b) as-prepared CuO particles

TGA curves

To evaluate the thermal stability of compounds against heat, the best technique is to use thermogravimetry analysis. The TGA curves of the complexes in the temperature range from 25 to 700 degrees are shown in Figure 7. Complex **1** does not lose much weight up to 100 °C, which indicates that the solvent has little crystallization or moisture, while complex **2** shows about 5% weight loss due to adsorption of solvent molecules. After that, both complexes show weight loss in two more stages. The first step is in the temperature range from 100 to 200 °C, which is a mass losses of $\approx 20\%$ for complex **1** and $\approx 6\%$ for complex **2**. The second stage in complex **1** occurs in the temperature range from 200 to 260

°C, in which about 40% of the mass of the compound is reduced. After that, complex **1** loses about 10% of its mass at a temperature from 260 to 700 °C. At 700 °C, complex **1** lost about 70% of its mass. The second stage in complex **2** occurs in the temperature range from 200 to 350 with the mass losses of about 35%. After that, from 350 to 470 °C, a mass loss of about 5% is seen for complex **2**. Then at 700 °C, complex **2** lost about 46% of its weight. Thermal results show that the thermal stability of complex **2** is much higher than that of complex **1**. This greater thermal stability of complex **2** means that the time required to prepare CuO particles from this complex is almost twice the time of formation of CuO particles from complex **1**.

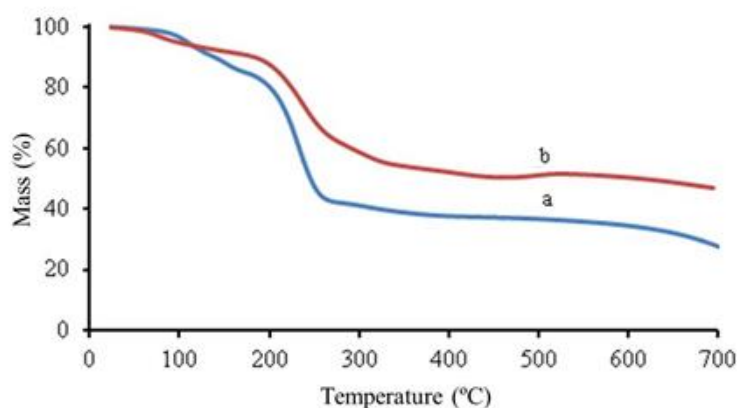


Figure 7: TGA curves of complex a) **1** and b) **2**

Antibacterial activities

The evaluation of the antibacterial effect of complexes and copper oxide nanoparticles prepared from them, conducted by measuring the

diameter of growth inhibition, is shown in Figure 8.

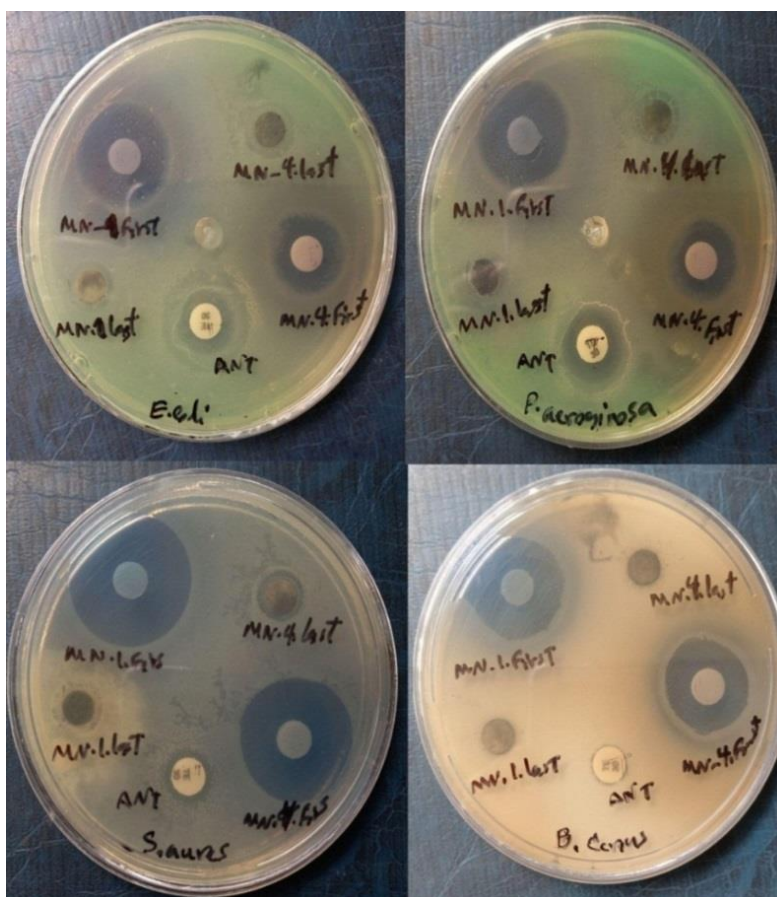


Figure 8: Antibacterial activity of complex 1 (MN.1.first), complex 2 (MN.4.first), CuO prepared from complex 1 (MN.1.last) and complex 2 (MN.4.last)

As shown in Figure 8, the complexes displayed better inhibitory effect when compared with the CuO particles against all tested bacteria strains. The agar diffusion test results of complexes 1 and 2 were better than the as-prepared CuO particles and also standard antibacterial drug. The better inhibitory effect of complexes than standard drug can be accounted for based on Tweedy's chelation [31,32]. The polarity of copper(II) ions was reduced by coordination of maleic acid as ligand, due to the overlap of the ligand orbital and partial sharing of the positive charge of the copper(I) ion. Then, the lipophilicity of the complexes increased. Consequently, the penetration of the complexes into lipid membranes increased, and resulted in blockage of metal sites in the enzymes of the microorganisms. The highest inhibition activity against all bacteria was observed for complex 1, followed by complex 2. It is evident that the changes in structure of the complexes led to the changes of the activities against the used pathogenic strains.

Conclusion

Two copper complexes were prepared using maleic acid as ligand and characterized. The thermal results of the complexes show that the complex 2 displays better thermal stability than 1. SEM images show that the particles of the complexes were agglomerated with different shapes and sizes. In addition, CuO particles were prepared by solid state thermal decomposition at 600 °C. The results of XRD and IR confirm the preparation of CuO particles. Furthermore, the antibacterial properties against two gram-negative bacteria and two gram-positive bacteria indicate that the as-prepared CuO particles did not have much activity, but the complexes show very good activity. The agar diffusion test results also show that the complexes have excellent antibacterial properties, suggesting the obtained complexes to be applied as antibacterial material in medical fields.

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Authors' contributions

All authors contributed toward data analysis, drafting and revising the paper and agreed to be responsible for all the aspects of this work.

Conflict of Interest

We have no conflicts of interest to disclose.

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