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ANTI-*Escherichia coli* NON-PATHOGENIC STRAIN ACTIVITY OF COMPLEX COMPOUND BASED ON COPPER(II) AND 2,4,5-TRIPHENYL-1*H*-IMIDAZOLE

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ABSTRACT

The complex of Copper(II) binding 2,4,5-triphenyl-1*H*-imidazole ligand is a new copper complex and exhibits therapeutic properties to bacteria. The present observation is focused on anti-Escherichia *coli* non-pathogenic strain using disc diffusion method. Copper(II)-2,4,5-triphenyl-1*H*-imidazole complex compound showed anti-*Escherichia coli* non-pathogenic strain activity with a range of inhibition zone 14.51-17.37 mm and compared with free metal Cu(II) less reactive with a range of inhibition zone 10.57-27.16 mm, but more no toxic in the Vero cells with CC_{50} 44.74 µg/ml.

Keywords: Copper(II), 2,4,5-triphenyl-1*H*-imidazole, Complex Compound, Antibacterial

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INTRODUCTION

2,4,5-triphenyl-1*H*-imidazole plays vital parts for supramolecular congregations since it can give a bidentate N-donor site for chelating with ions of the metal to create bridge ligands, imidazole is a five-membered ring aromatic compound. It is composed of 3 carbon atoms and 2 nitrogen atoms.[1,2,3] Imidazole derivatives are known to possess desirable antibacterial,[4-8] antifungal,[6] anticancer,[9-11] and antiviral properties,[12,13] also 2,4,5-triphenyl-1*H*-imidazole are exceptionally imperative ligands in organometallic chemistry. Moreover, a few of their complexes bind to DNA. Imidazole antibiotic is pharmaceuticals that are commonly used in human medications and veterinary drugs.[14] Imidazole 2-aldoximes derivatives were reported anti-*Escherichia coli* with inhibition zone from 12.4 ± 0.71 to 21.8 ± 0.9 mm).[15]

The importance of metal ions in the vital function of living organisms, from mammalians to bacteria, has been widely recognized. They are incorporated into enzymes and cofactors that are required for various life processes. Copper is a basic following component for numerous organic forms, found in enzyme assortment, counting the copper centers of cytochrome C oxidase, the Cu-Zn-containing superoxide dismutase enzyme, and it is the central metal within the oxygen-carrying hemocyanin pigment.[16] Growth inhibitory effects on common urinary pathogens have been reported, but uropathogenic *Escherichia coli* (UPEC) are less sensitive to nitric oxide than non-pathogenic strains of *Escherichia coli.*[17]

In general, the synthesized metal complexes have higher activities of biological to free ligands. Metal complexes excessively aggravate the respiratory process of cells and enhance the fusion of proteins, limiting aiding the development of life forms. In this study, the azomethine linkage (-C=N-) within the synthesized complexes displays broad natural action due to expanding the molecules liposolubility in microorganism crossing cell membrane.[18]

The new copper complex has been the significant focus of investigating efforts because too many important biological processes involve metal ions. Recently, complex copper(II) with 2,4,5-triphenyl-1*H*-imidazole exhibits broad therapeutic properties such as anti-breast cancer[19] and anti-dengue virus type 2.[20] However, in this experiment we herein report the antibacterial activity with*in vitro* method of copper(II)-2,4,5-triphenyl-1*H*-imidazole complex compound, especially for non-pathogenic strains of *Escherichia coli*.

EXPERIMENTAL

Material and Methods

Copper(II)-2,4,5-triphenyl-1*H*-imidazole complex compound was synthesized by previous publication[14] and $CuCl_2.2H_2O$ 99.0% (Merck, Germany) and bacterial *Escherichia coli* ATCC®25922™. Dimethylformamide (DMF) (Merck, Germany) was used for the dissolution of the compound and control.

General Procedure

Antibacterial activity of copper(II)-2,4,5-triphenyl-1*H*-imidazole complex compound and $CuCl_2.2H_2O$ were tested against non-pathogenic strains of *Escherichia coli* in Muller Hinton Agar with disc diffusion method, using 10 ml of suspension containing bacteria $1.5x10^8$ CFU/ml. The discs (6 mm in diameter) were added with the 20 µl/disc solutions of the compound. The various concentrations of each compound were 50 mg/ml, 75 mg/ml, 125 mg/ml, 250 mg/ml, and 500 mg/ml. Negative controls were used by the DMF. The plates of inoculation were kept at 37 °C for 24 h.[21] Activity of antibacterial was assessed by measuring the inhibition zone against the test organisms using calipers millimeter scale. Four replications were performed in this test.

Statistical Analysis

The standard deviation was performed using Microsoft Excel 2010.

RESULTS AND DISCUSSION

Copper(II)-2,4,5-triphenyl-1*H*-imidazole and $CuCl_2.2H_2O$ were tested for anti- *Escherichia coli* activity with McFarland standard. The activity was resolved to make the use of a disk diffusion method with various concentrations of compound, 50 mg/ml, 75 mg/ml, 125 mg/ml, 250 mg/ml, and 500 mg/ml in DMF as a solvent. The investigation results were compared with DMF as a negative control and expressed in terms of mm. As the extract concentration increases, the inhibition zone increases. Inhibition zones were shown in Table-1 and the standard deviation curve in Fig.-1.

Table-1: Inhibition Zone of Copper (II)-2,4,5-triphenyl-1*H*-imidazole and $CuCl_2.2H_2O$ against *Escherichia coli*

Concentration of Compound (mg/ml)	Inhibitions Zone (mm)	
	Copper(II)-2,4,5-triphenyl-1*H*-imidazole	$CuCl_2.2H_2O$
50	14.51	10.57
75	14.88	15.77
125	15.24	20.60
250	16.22	25.75
500	17.37	27.16
DMF	no inhibition zone	no inhibition zone

In general, the $CuCl_2.2H_2O$ displayed a better inhibitor effect compared to the Copper(II)-2,4,5-triphenyl-1*H*-imidazole complex compound against *Escherichia coli* with the range of 10.57-27.16 mm. In the previous study, $CuCl_2.2H_2O$ effects on Vero cells (CC_{50}) up to 5.03 µg/ml[22] and Copper(II)-2,4,5-triphenyl-1*H*-imidazole up to 44.74 µg/ml[20] were reported. Free metal has greater polarizability than that complex compound because it contains more electrons and the free metal produced more ions soluble in water.[23] This effect causes $CuCl_2.2H_2O$ to be more toxic because free metal ions in the medium are more numerous, so it damages the cell wall faster than a complex compound that has high stability such as copper(II)-2,4,5-triphenyl-1*H*-imidazole.

In a previous study about Cu(II) complex with N-(5-cloro-2-hydroxyphenyl)-3-methoxy-salicylaldimine ligand was reported to have no activity on *Staphylococcus epidermidis*. The Cu(II) complex activity can be clarified with its dissociation in a solvent; the Cu(II) complex dissociation can be described as an

important factor of the antimicrobial activity.[24].Not only Cu(II) complex compound with 4-(5-nitrofurfuralideamino)-5-mercapto-3-methyl-1,2,4-triazole, but also the complex compound of Cu(II)-4-bromo-2-(1*H*-imidazo[4,5-f][1,10]phenanthroline-2-yl)phenol was also reported activity of *Escherichia coli.*[25,26]

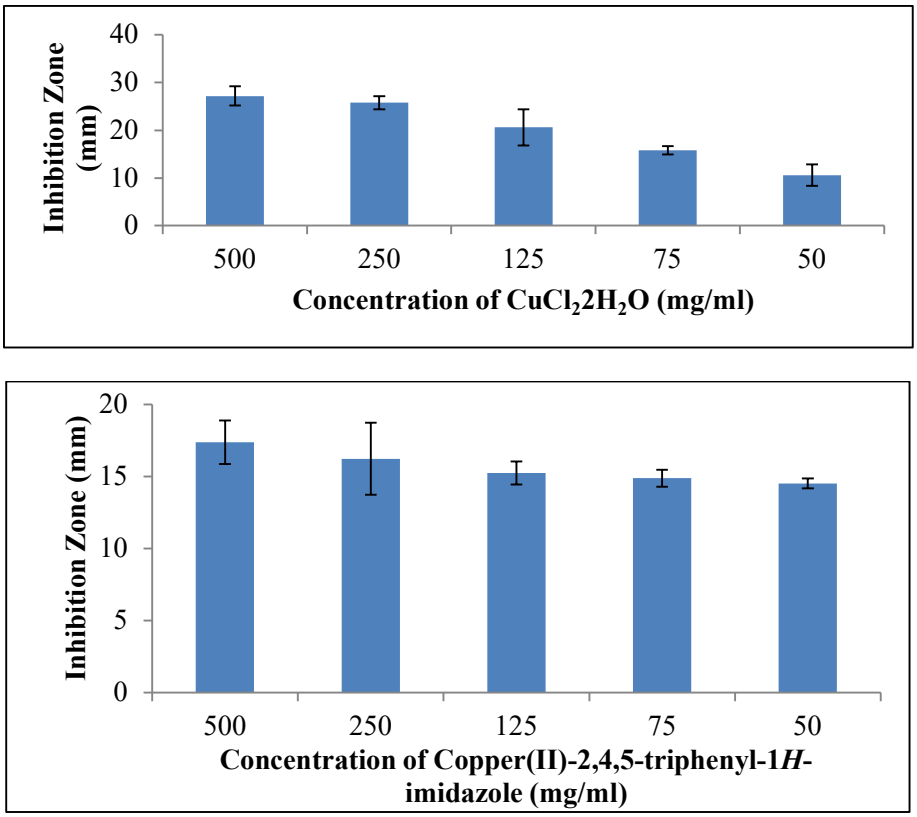

Fig.-1: Standard Deviation of Anti-*Escherichia coli* Activity of $CuCl_2.2H_2O$ and Copper(II)-2,4,5-triphenyl-1*H*-imidazole Complex Compound with Various Concentration

Chelation or coordination also reduces the polarity of the ion of metal since the partial sharing of its positive charge with these donor groups and conceivably the π-electron delocalization inside the total chelate ring framework. Moreover, the process of chelation decreases the central metal atom hydrophilic nature, which is in turn, supports its permeation through the membrane lipid layer, therefore, causing the complex compound to cross the cell wall membrane and increases its microorganism activity.[27]

CONCLUSION

Copper(II)-2,4,5-triphenyl-1*H*-imidazole complex compound and $CuCl_2.2H_2O$ showed anti- *Escherichia coli* activity. $CuCl_2.2H_2O$ performed the highest inhibition zone than Copper(II)-2,4,5-triphenyl-1*H*-imidazole complex compound, but it is more toxic to Vero cells. This result is preliminary and is starting for further investigations.

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