Computational Approach to Evaluate Eugenol Affinity and Derivatives Empirical Against Cu(II)

Muhammad Cholid Djunaidi[1*], Tantri Nevi Astuti[1], Parsaoran Siahaan[1]

[1]Chemistry Department, Faculty of Natural Sciences and Mathematics, Diponegoro University
Jl. Prof. Soedarto, Tembalang, Semarang, Indonesia

*Corresponding author email: muhammadcholiddjunaidi@gmail.com

ABSTRACT. A computational approach to assess the emperical results of eugenol affinity, eugenoxy acetate (EOA), and pyridine methyl eugenoxy acetate (PMEOA) against Cu^{2+} has been done. This research aims to determine the effects of the functional groups ($-OH$, $-COOH$, and $-N$) on eugenol and their derivatives on the selectivity of Cu^{2+} adsorption experimentally and to calculate the energy interaction between eugenol compounds and derivatives with Cu^{2+}. The experimental approach was carried out by solvent extraction method, using 10 mL of Cu^{2+} 10 ppm solution along with 0.3089 mmol of eugenol, EOA and PMEOA. The remaining concentration of Cu^{2+} metal after extraction in the water phase was measured using an Atomic Absorption Spectrophotometer (AAS). Assessments of the Cu^{2+} metal interaction with eugenol, EOA and PMEOA compounds were carried out using the ab initio method with 6-31G** basis set to predict the interaction energy. The results showed that pyridine methyl eugenoxy acetate (PMEOA) can separate Cu^{2+} better than eugenol and EOA with extraction efficiency (% E) = 78.76%. The calculation results of Cu^{2+} metal interactions with eugenol, EOA, and PMEOA compounds found that PMEOA has the lowest energy of interaction compared to eugenol and EOA with Cu^{2+} metal.

Keywords: Eugenol, Eugenol Derivatives, AAS, Ab Initio, *affinity, Cu^{2+}, solvent extraction*

INTRODUCTION

The industry is currently experiencing very rapid development. However, the result of the rapid development of the industry is the production of waste in the form of solid, liquid and gas wastes which result in environmental pollution. Liquid waste in the industry has a role in the release of heavy metals into the water flow. This creates a negative impact on living things in the environment. One of the heavy metals that can pollute the environment is Cu. Metal Cu above the permitted threshold will cause poisoning to living things, especially in humans, potentially causing death. Therefore, it is necessary to tackle pollution caused by Cu metal. Efforts to control and process heavy metal waste are developing, leading to the searches for new methods that are cheap, effective and efficient (Kundari & Slamet, 2008).

A method that can be used to process heavy metal waste is liquid-liquid extraction. Extraction is highly significant in selective metal separation techniques in industrial waste treatment processes (Khoutoul et al., 2016). Liquid-liquid extraction is the commended technique to recover metals (Hamzah et al., 2011). Moreover, the chosen extraction method has advantages in its use as it does not require expensive and complicated equipment (Harimu, Matsjeh, Siswanta, & Santosa, 2009). The basic principle of liquid-liquid extraction involves contacting a solution with other solvents that are not immiscible with the original solvent with different density so that it will form two phases shortly after the solvents are combined (Mirwan & Wicakso, 2008)

The latest development of extraction separation method tends to increase selectivity to certain metals by finding new ligands as extractants through compound synthesis (Kakoi et al., 1998). One of the raw materials that can be used is eugenol. Eugenol is a natural component found in essential oils, including cloves. The content of eugenol in cloves ranges from 60-90% (Sneddon, 1997). Eugenol is an Indonesian natural ingredient that can be used for the separation of metal ions (Djunaidi, Jumina, Siswanta, & Ulbricht, 2015; Djunaidi, Siswanta, & Jumina, 2015). Eugenol is used as a starting material for the synthesis of a compound because there are three functional groups that are bound to it, namely the allyl, hydroxyl and methoxy groups that can potentially work as functional monomers for the selective adsorption process of Cu (Djunaidi, Wibawa, & Murti, 2018). With these three active groups, eugenol can function as a carrier

through a hydroxyl group where eugenol can be entered into a more selective functional group. To increase the selectivity of eugenol, modification was carried out to improve the selectivity of eugenol (Djunaidi, Khabibi, & Khrisna, 2010). In this study, modification was done by synthesizing eugenol derivatives in the form of eugenoxy acetic acid (EOA) and pyridine methyl eugenoxy acetate (PMEOA).

In addition to the synthesis of eugenol derivatives, this study also aims to study the interaction of Cu^{2+} with eugenol, EOA, and PMEOA molecules, calculate the interaction energy between eugenol compounds and eugenol derivatives with the most stable Cu^{2+} in silico. The experimental approach is carried out by solvent extraction methods. The concentration of Cu^{2+} metal remaining after extraction in the liquid phase was measured using Atomic Absorption Spectrophotometer (AAS). Evaluation of the interactions of Cu^{2+} metal with eugenol, EOA, and PMEOA compounds were carried out using the ab initio method with basis set 6-31G ** to predict the interaction energy. Through the ab initio method in this study, computational prediction of the interactions can be found and compared to existing theories and experimental results.

EXPERIMENTAL SECTION
Materials
Eugenol pa (SIGMA Aldrich), technical grade Na_2SO_4 (Merck), HCl (Merck), $NaHCO_3$ (Merck), NaOH pa (Merck), $ClCH_2COOH$ pa (Merck), Chloroform pa (Merck), Aqua Bidest, $Cu(NO_3)_2$ (Merck), 2- Pyridinemethanol pa (SIGMA Aldrich), Thionyl Chloride pa (Merck).

Instruments
Laboratory glassware, reflux equipment, analytical balance sheet (Mettler-200), magnetic stirrer, hotplate stirrer, spatula, pH meter, fine filtering paper, AAS (Perkin Elmer), FTIR (8201PC Shimadzu), a set of computers with Linux and Windows OS, Notepad ++ software, Chemcraft Software, and Nwchem 6.3 software.

Methodology
Eugenoxy Acetic Acid Synthesis
Five grams of eugenol were put into a 100 mL boiling flask and was added with 17.5 mL of 33% NaOH solution. The mixture was stirred for 30 minutes. Then 12.5 mL of 50% chloroacetic acid solution was added gradually using a dropping pipette while it continued to be stirred. The mixture was heated in a water bath at a temperature of 80-90 °C. Heating was carried out for 2 hours and the process proceeded to cooling and acidification using 6 M HCl to obtain pH=1. The next stage was extraction using 50 mL

diethyleter with 2 repetitions. The ether extracted was combined and extracted again using sodium bicarbonate 5% b/v as much as 30 mL with 3 repetition. The layer of water was then acidified with 6 M HCl to attain pH=1. Filtering, drying, and weighing were carried out. The results obtained were analyzed using FTIR.

Pyridine Methyl Eugenoxy Acetate Synthesis
A total of 3 g (0.0135 mol) of eugenoxy acetic acid (EOA) was put into a 100 mL boiling flask. The EOA was added with 1.6 mL (2.624 g, 0.022 mol) thionyl chloride dropwise. Then the mixture was refluxed for 150 minutes in a warm cooking oil bath (40 °C), and then cooled. Into the mixture 2 mL (2.262 g, 0.0207 mol) of pyridylcarbinol was added dropwise and refluxed again in warm cooking oil (40 °C) for 60 minutes. After it had cooled the result obtained was dissolved in chloroform and washed with water. The extraction result was dried with sodium sulfate anhydride, filtered and then evaporated to remove the remaining solvent. Furthermore, the results were analyzed using FTIR.

Liquid-liquid Extraction
A sample with a concentration of 0.000638 mol was dissolved in 10 mL of chloroform and extracted with 10 mL of 10 ppm Cu(II) ion for 3 hours. The mixture was separated and the Cu(II) concentration in the filtrate was analyzed using AAS twice.

Computational Method
Nwchem 6.3 program was used for all *ab initio* molecular orbital and self-consistent field calculations. The geometry of eugenol, EOA and PMEOA, and Cu^{2+} metal ions were optimized at the 6-31G** basis set. The energy of intermolecular interactions of molecules was also calculated by the SCF method with the same basis for the *ab initio* calculation.

RESULTS AND DISCUSSION
Eugenoxy Acetic Acid (EOA) Synthesis
The results of the analysis using an infrared spectrometer were obtained according to **Figure 1**. The presence of absorption bands at 3400 and 3500 cm^{-1} indicate the presence of −OH groups in carboxylic acids. Absorption bands in the range 3100-3000 cm^{-1} are C−H sp bands, the range 1600-1475 cm^{-1} is vibrations of C=C from the aromatic ring and the range 800-900 cm^{-1} indicates that the aromatic is substituted. Uptake at 1635 cm^{-1}, 997 cm^{-1}, and 915 cm^{-1} are the absorption of vinyl groups (RHC = CH). Acid carbonyl groups are shown in absorption at 1728.22 cm^{-1}.
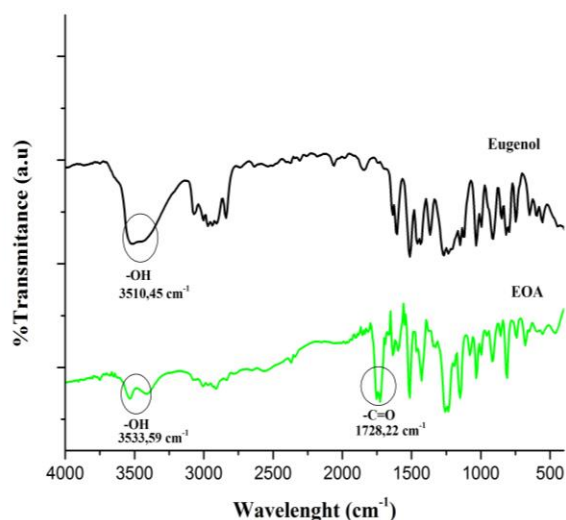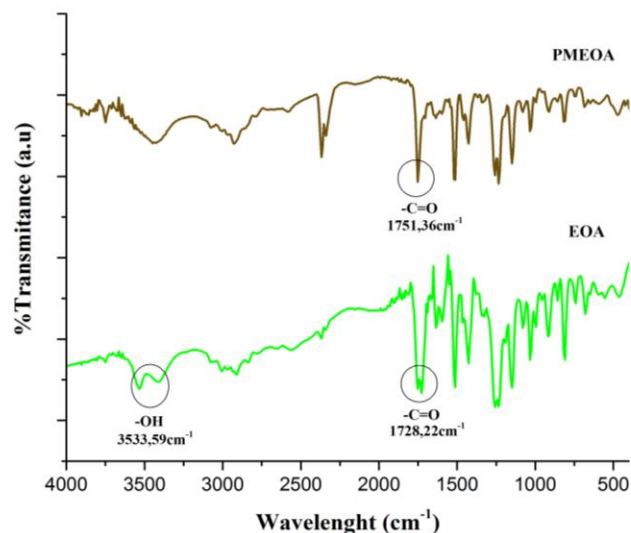
Figure 1. FTIR Spectra of Eugenol and EOA

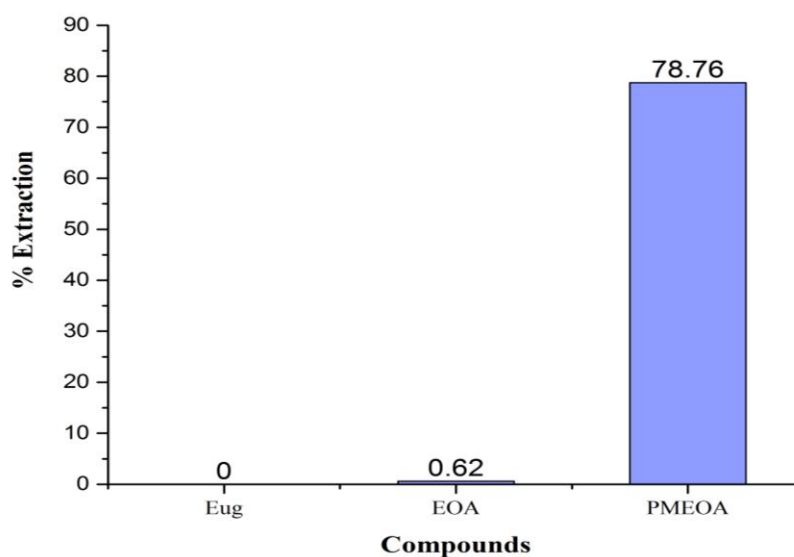**Figure 2**. FTIR Spectra of EOA and PMEOA

Figure 3. Results of Cu^{2+} metal % Extracted in Eugenol, EOA, and PMEOA

EOA was purified by extraction using diethyleter to remove polar impurities along with extraction using $NaHCO_3$ to remove nonpolar impurities. The synthesized EOA has a yield of 75.73%, in the form of a brownish white precipitate and has a melting point of 88-93 °C. The results of the EOA synthesis produced are in accordance with previous studies (Djunaidi et al., 2010).

Pyridine Methyl Eugenoxy Acetate (PMEOA) Synthesis

PMEOA was obtained from EOA basedsynthesis. The results of PMEOA synthesis can be seen from the results of the following FTIR analysis, **Figure 2**. The

formation of ester can be identified from the infrared spectra at wave number 1751,36 cm^{-1} which is a spectrum of the carbonyl ester group. Another proof of the formation of esters is the loss of characteristic spectra of the −OH group or hydrogen bonds which form a wide band at a wavenumber of about 3500 cm^{-1} (Djunaidi et al., 2018). The experiment obtained PMEOA with a yield of 75,73%.

Cu^{2+} Metal Extraction Results

From the experimental outcome obtained, %extracted results are shown in **Figure 3**. Based on **Figure 3** above, it appears that the percentage of Cu(II)

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metal ions extracted was highest in PMEOA, followed by EOA and last, eugenol. This is in accordance with the HSAB (Hard Soft Acid Base) theory that says hard acid metals bind more strongly with hard bases, soft acids with soft bases, and borderline acids with borderline bases. Cu(II) is a borderline acid metal ion so that it can bind to the N-active ligand which is a stronger borderline base than other metal ions (Ho, 1975).
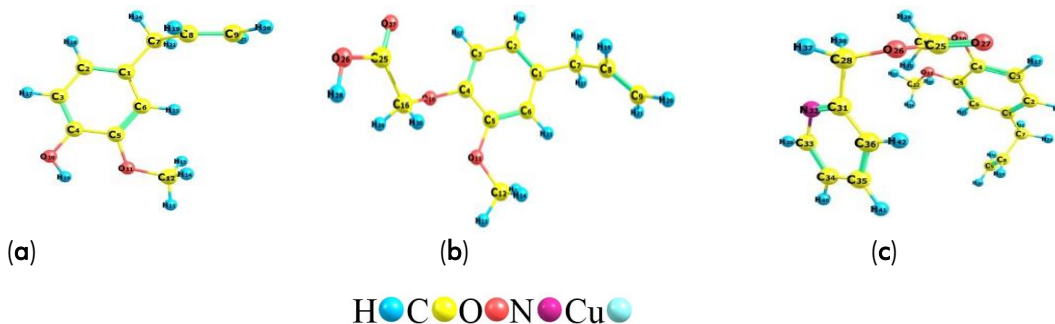
Figure 4. (a) Optimized Geometry of Eugenol (b) Eugenoxy Acetate (EOA) (c) Pyridine Methyl Eugenoxy Acetate
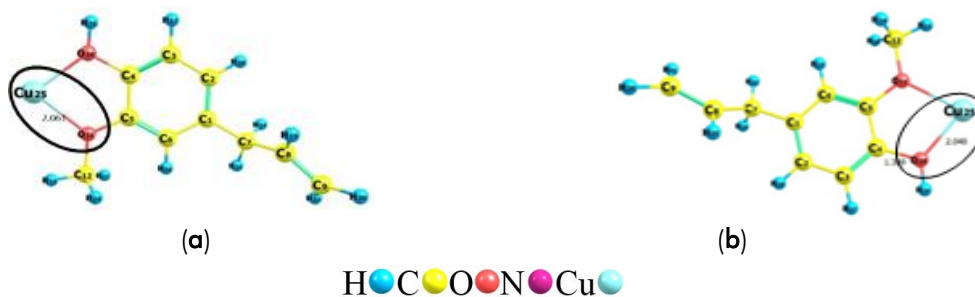
Figure 5. Optimized Geometry of interaction between Eugenol and ..Cu^{2+} (a) Eugenol O_{10} atom ..Cu^{2+} (b) Eugenol O_{11} atom ...Cu^{2+}
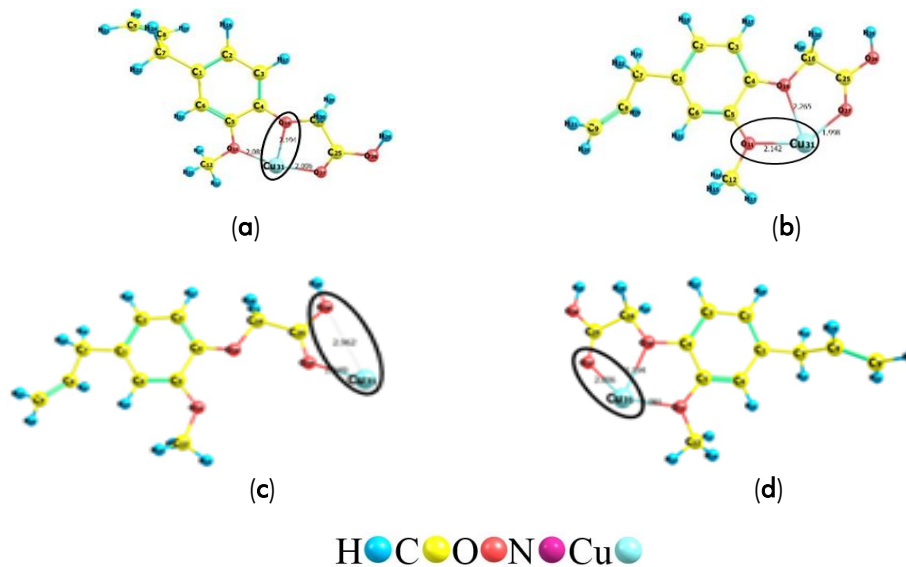
Figure 6. Geometry optimization of eugenoxy acetate (EOA) that has interacted with Cu^{2+} (a) EOA O_{10} atom Cu^{2+} (b) EOA O_{11} atom… Cu^{2+} (c) EOA O_{26} atom… Cu^{2+} (d) EOA O_{27} atom… Cu^{2+}

Computational Study

In this study, Cu^{2+} was exposed and interacted with eugenol, EOA, and PMEOA molecules. The atoms that interacted with Cu^{2+} in eugenol were O_{10} and O_{11}, in EOA were O_{10}, O_{11}, O_{26} and O_{27} whereas in PMEOA were O_{10}, O_{11}, O_{26}, O_{27}, and N_{32} atoms. The results of geometry optimization show that there are interactions between Cu^{2+} with eugenol, EOA and PMEOA, **Figure 4**. and **Table 1**, which were indicated by changes in distance, angle, and dihedral in each molecule shown in **Table 2**.

The interactions were carried out at the positions of the eugenol O_{10} atom ..Cu^{2+} and eugenol O_{11} atom ...Cu^{2+} which produced interaction energies that are not much different, specifically O_{10} ...Cu^{2+} at -766.554 kJ/mol and O_{11} ...Cu^{2+} at -766.523 kJ/mol. Energy of the resulting interactions is not much different because ...Cu^{2+} interacts with O_{10} and O_{11} producing energies that are not much different. However, the stability generated from the O_{10} atomic interaction with Cu^{2+} tends to be greater because O_{11} has a larger steric effect thus ...Cu^{2+} interacts better with O_{10} (**Figure 5.b**) (Warren, 1981).

The interactions that occur in the EOA molecule take place in the positions of O^{10}...Cu^{2+}, O_{11}...Cu^{2+}, O_{26}...Cu^{2+}, O_{27}...Cu^{2+} which produced energy of interactions of -879.662 kJ/mol, -877.986 kJ/mol, -859.391 kJ/mol, and -879.661 kJ/mol, respectively. Geometry optimizations of interaction structures obtained the most stable energy in the interaction of O_{10} EOA atom with ...Cu^{2+} as it has the greatest interaction energy compared to the others (Zhai et al., 2018). This is because in that position Cu^{2+} interacts a lot more creating stronger interaction (**Figure 6.a**).

Molecular interaction positions between PMEOA and Cu^{2+} namely O_{10}...Cu^{2+}, O_{11}...Cu^{2+}, O_{26}...Cu^{2+}, and O_{27}...Cu^{2+} produced interaction energies of -1042.046 kJ/mol, -1042.044 kJ/mol, -990.714 kJ/mol, -912.450 kJ/mol and -995.279 kJ/mol, respectively. The greatest interaction energy sign on the molecular geometry optimization results states stable molecular structure (Yopianto, et al., 2011). Accordingly, the most powerful interaction of the PMEOA molecule is at the position O_{10}...Cu^{2+} as it produces the greatest interaction energy (**Figure 7.a**).

(a)   (b)   (c)

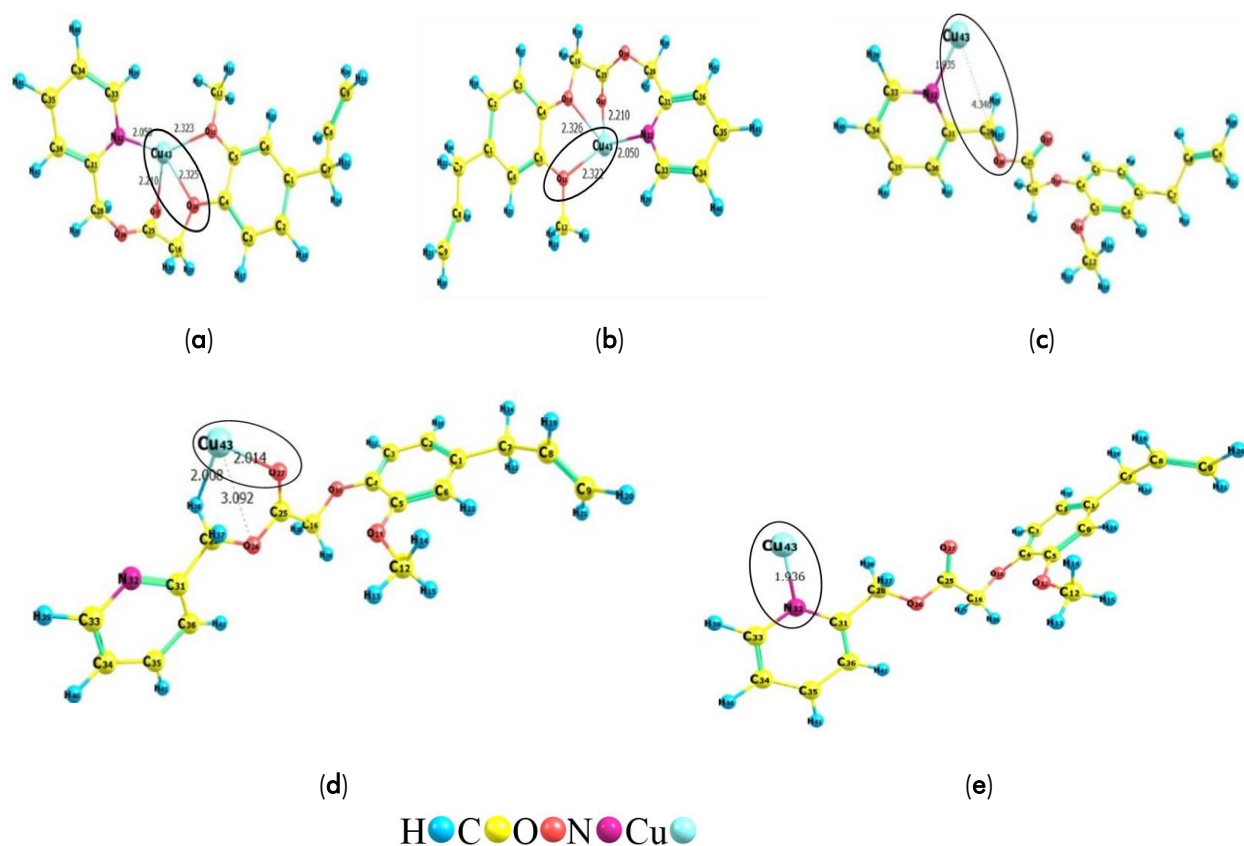(d)   (e)

H ● C ● O ● N ● Cu ●

Figure 7. Geometry optimization of pyridine methyl eugenoxy acetate (PMEOA) that has interacted with Cu^{2+} in positions (**a**) PMEOA O_{10} atom ...Cu^{2+} (**b**) PMEOA O_{11} atom...Cu^{2+} (**c**) PMEOA O_{26} atom...Cu^{2+} (**d**) PMEOA O_{27} atom...Cu^{2+} (**e**) PMEOA N_{32} atom ...Cu^{2+}

Table 1. Bond length, angle, and energy obtained from geometry optimization of molecular interaction structure.

Complexes	Bond length	(Å)	Bond angle	Degree	Energy (kJ/mol)
Eugenol	$Cu_{25}...O_{10}$	2.04774	C_4-$O_{10}...Cu_{25}$	113.57918	-766.554
	$Cu_{25}...O_{11}$	2.0613	C_5-$O_{11}...Cu_{25}$	113.68029	-766.523
EOA	$Cu_{31}...O_{10}$	2.19375	C_4-$O_{10}...Cu_{31}$	115.13062	-879.662
	$Cu_{31}...O_{11}$	2.14228	C_5-$O_{11}...Cu_{31}$	122.29807	-877.986
	$Cu_{31}...O_{26}$	2.96157	C_{25}-$O_{26}...Cu_{31}$	69.98086	-859.391
	$Cu_{31}...O_{27}$	2.00613	C_{25}-$O_{27}...Cu_{31}$	120.98512	-879.661
PMEOA	$Cu_{43}...O_{10}$	2.32538	C_5-$O_{10}...Cu_{43}$	88.73277	-1042.046
	$Cu_{43}...O_{11}$	2.32166	C_5-$O_{11}...Cu_{43}$	122.84923	-1042.044
	$Cu_{43}...O_{26}$	4.34555	C_{25}-$O_{26}...Cu_{43}$	115.37284	-990.714
	$Cu_{43}...O_{27}$	2.0138	C_{25}-$O_{27}...Cu_{43}$	122.82326	-912.450
	$Cu_{43}...N_{32}$	1.935510	C_{31}-$N_{32}...Cu_{43}$	121.54048	-995.279

Table 2. Comparison of bond length, angle and dihedral results from geometry optimization of molecular structure

Molecule	Bond length	(Å)	Bond angle	Degree	Torsion Angles	Degree
Eugenol						
Optimization	O_{10}-C_4	1.34861	C_3-C_4-O_{10}	120.1614	C_2-C_3-C_4-O_{10}	179.9665
	O_{11}-C_5	1.35878	C_4-C_5-O_{11}	114.1238	C_3-C_4-C_5-O_{11}	179.9422
Interaction						
Configuration 1	O_{10}-C_4	1.36927	C_3-C_4-O_{10}	122.3264	C_2-C_3-C_4-O_{10}	-179.273
Configuration 2	O_{11}-C_5	1.36581	C_4-C_5-O_{11}	116.2912	C_3-C_4-C_5-O_{11}	-179.408
EOA						
Optimization	O_{10}-C_4	1.36849	C_3-C_4-O_{10}	120.0898	C_2-C_3-C_4-O_{10}	-176.416
	O_{11}-C_5	1.35068	C_4-C_5-O_{11}	115.9893	C_3-C_4-C_5-O_{11}	179.6043
	O_{26}-C_{25}	1.33661	C_{16}-C_{25}-O_{27}	113.7281	O_{10}-C_{16}-C_{25}-O_{27}	179.4115
	O_{27}-C_{25}	1.17834	C_{16}-C_{25}-O_{27}	125.3131	O_{10}-C_{16}-C_{25}-O_{27}	-0.00411
Interaction						
Configuration 1	O_{10}-C_4	1.35951	C_3-C_4-O_{10}	124.1649	C_2-C_3-C_4-O_{10}	179.0462
Configuration 2	O_{11}-C_5	1.32628	C_4-C_5-O_{11}	114.8564	C_3-C_4-C_5-O_{11}	-179.701
Configuration 3	O_{26}-C_{25}	1.30246	C_{16}-C_{25}-O_{27}	116.9226	O_{10}-C_{16}-C_{25}-O_{27}	-179.976
Configuration 4	O_{27}-C_{25}	1.19695	C_{16}-C_{25}-O_{27}	121.7505	O_{10}-C_{16}-C_{25}-O_{27}	-6.13855
PMEOA						
Optimization	O_{10}-C_4	1.36678	C_3-C_4-O_{10}	120.0927	C_2-C_3-C_4-O_{10}	-176.327
	O_{11}-C_5	1.34967	C_4-C_5-O_{11}	115.9279	C_3-C_4-C_5-O_{11}	-179.991
	O_{26}-C_{25}	1.33915	C_{16}-C_{25}-O_{27}	117.1841	O_{10}-C_{16}-C_{25}-O_{27}	178.6205
	O_{27}-C_{25}	1.18047	C_{16}-C_{25}-O_{27}	123.6502	O_{10}-C_{16}-C_{25}-O_{27}	0,55763
	N_{32}-C_{31}	1.32213	C_{28}-C_{31}-N_{32}	114.7156	O_{26}-C_{28}-C_{31}-N_{32}	-159,967
Interaction						
Configuration 1	O_{10}-C_4	1.30288	C_3-C_4-O_{10}	126.0435	C_2-C_3-C_4-O_{10}	-179.452
Configuration 2	O_{11}-C_5	1.32027	C_4-C_5-O_{11}	114.2208	C_3-C_4-C_5-O_{11}	179.0307
Configuration 3	O_{26}-C_{25}	1.32519	C_{16}-C_{25}-O_{27}	110.3717	O_{10}-C_{16}-C_{25}-O_{27}	163.4247
Configuration 4	O_{27}-C_{25}	1.20661	C_{16}-C_{25}-O_{27}	124.4902	O_{10}-C_{16}-C_{25}-O_{27}	-3.36745
Configuration 5	N_{32}-C_{31}	1.33613	C_{28}-C_{31}-N_{32}	113.6548	O_{26}-C_{28}-C_{31}-N_{32}	-166.615

Tabel 3. Energy Optimization of molecular structure with interactions of molecules and without molecular interactions

Molecule	Energy (kJ/mol)					
	Configuration 1	Configuration 2	Configuration 3	Configuration 4	Configuration 5	Optimization
Eugenol	-5706420.41	-5706420.379				-5705653.856
EOA	-6301540.971	-6301539.295	-6301520.701	-6301540.971		-6300661.31
PMEOA	-7048798.877	-7048845.643	-7048845.642	-7048794.311	-7048716.047	-7047803.598

As a result of the interaction, there is a change in the geometrical structure of the molecules. The changes can include the dihedral angle and the energy. The results of the calculations are presented in **Table 3** where the molecules that had been interacted with Cu^{2+} are more stable than the molecules that had not. This is demonstrated by the energy produced by the Cu^{2+}-interacting molecules that is lower than the molecules that have not been interacted with Cu^{2+}. In particular, the most stable molecule was the PMEOA $Cu_{43}...O_{10}$ molecule with the lowest energy produced compared to the other molecules is shown in **Table 3**.

CONCLUSIONS

This study has confirmed the experimental results of the extraction of Cu metal ion with eugenol and its derivatives (EOA, PMEOA) with computational studies. Experimental results of eugenol and synthesis of eugenol derivatives in the form of EOA and PMEOA were applied to extract Cu^{2+}. Empirically the PMEOA was the best in extracting Cu^{2+} exceeding eugenol and EOA proven by the percentage of Cu^{2+} extracted in PMEOA, EOA and eugenol at 78.76%, 0.62%, and 0% respectively. Experimental results are supported by computational studies in which the most negative interaction energy generated comes from the PMEOA molecule. Thus it can be concluded that PMEOA is the most stable molecule in creating interaction with Cu^{2+}.

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