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Synthesis and Characterization of Copper (II) Complexes with Various Ligands and its Larvicidal, Antifeedant and Mosquito Larval Growth and Regulation Activities

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Abstract

The catalyst free one-pot synthesis of Copper complexes with various organic ligands by using ethanol as a solvent. This method offers efficient and mild reaction conditions. The synthesized complexes were described by UV- Visible and FT-IR spectroscopy.The synthesized complexes are also evaluated for larvicidal, antifeedant, and mosquito larval growth and regulation activities. Complex**1b** was highly active against Culexquin quefasciatusthan complexes **1a**and **1c**with the LD_{50} value of 45.28 µg/mL. The complexess **1a**and **1c**were less active against Culexquin quefasciatus with the LD_{50} values of 69.83 and 84.73 µg/ml respectively. Complex **1a** produced 66% mortality in 24hr at 100 µg/ml againstOreochromis mossambicus in antifeedantscreening and also toxicity was measured as death percentage at 24hr. Complex **1b** produced 60% mortality in 24hr at 100 µg/ml. Among the synthesized complexes **1a-1c** the complex **1a** havinghightoxicity with the LD_{50} value of 69.57 µg/ml.

Keywords: Copper complexes, Culexquin quefasciatus, Larvicidal activity, Antifeedant activity.

Introduction

Copper displayssignificant biological action whichever as acrucialdrop metal or as a fundamental of numerousexogenously directedmixes in individuals. Theearliercharacterof copper was destined to albumin, ceruloplasmin, and also formerproteins, whereas in later it is assured to various types of ligands for complex formation that interrelate with biomolecules,mostlynucleic acids and proteins. The multidimensionalcharacter of copper in bioticorganisms is validated by more than a fewstudies. In precise the contribution of copper in humanoidinfections has been defined from a remedial-chemical [1]and a biochemical view [2] concentrating on the molecular functioning of Cu conveyance [3].Overexistinginvestigationexertion is mentioned on copper homeostasis [4] and its kin to ironmetabolism [5] in addition to the part of copper in naturalproceduresinterrelated to human pathology and physiology [6, 7].

Copper (II) complexes have a critical function in the active sites of many metalloenzymes in live creatures and have the potential to be used in a wide range of catalytic processes in live organisms, including electron transfer processes and the stimulation of certain anticancer compounds [8]. Bioinorganic [9] and medicinal chemistry [10] both use the above-mentioned advancements. Furthermore, copper (II) chelates were developed to interact with biological

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processes and show anticancer, antibacterial, antineoplastic, and antifungal properties [11–13]. Because of their high DNA base pair binding capability, certain copper (II) N, N and N,S,O promoter chelators are important anticancer moieties [17].Metal chelates have already been employed as DNA structural probes in solutions, as reagents for mediating double DNA strand cleavage, and also as chemotherapy drugs [18–27].Recentattention in copper complexes is restricting from itsprospectiveusage as enzyme inhibitors, anti-inflammatory, antimicrobial, chemical nucleases,antitumor agents, or antiviral. Keeping this in mind the present work focusses the synthesis of various copper complexes and evaluated for its larvicidal, antifeedant and mosquito larval growth and regulation activities.

Experimental

Chemicals and reagents

Chemicals were bought from local suppliers and used as received. Pre-coated silica gel plates were used for TLC analysis. Melting points were noted in open capillary tubes and were uncorrected.Shimadzu UV - 1280 spectrometer with the ranges between 200-800 nm was used to record the UV-Visible spectraof complexes. Shimadzu 8201pc spectrometer with the ranges between 4000-400 cm^{-1} was used to record the FT-IR spectra of complexes.

Synthesis of Bis-(N-aminoethylethanolamine)-Copper (II) Complex (1a).

The compounds N-aminoethylethanolamine (0.02mol, 2ml) in 5ml ethanol is stirred in a magnetic stirrer with $CuCl_2.2H_2O$ (0.01mol, 1.7g) in 5ml ethanol for one hour. Blue coloured precipitate was formed. The solvent ethanol was evaporated under vacuum. The termination of the reaction was confirmed by TLC technique. The crude product was recrystallized in hot alcohol for further purification purpose.

Bis-(N-aminoethylethanolamine)-Copper (II) chloride(1a).

Blue solid; mw: 398.86; mp 195°C**;** UV λ^{MeOH}_{max} nm (abs): 225 (0.65), 253 (0.79), 591 (0.02);IR (cm^{-1}): 3759.70 (OH), 3410.74 (NH), 2922.91 (CH), 1474.46 (C-N) 1018.83 (C-O), 745.22 (CHbend) 670.80 (Disubstituted); Elemental analysis**:** Calculated. For: $C_{12}H_{32}Cl_2CuN_4O_2$: C, 36.14; H, 8.09; N, 14.05 %; Found: C, 36.12; H, 8.10; N, 14.06; %

Synthesis of Bis-(4-benzylidene-3-methyl-1H-pyrazol-5(4H)-one)-Copper (II) complex (1b).

The compounds 3-methyl-1H-pyrazol-5(4H)-one (0.01mol, 0.98) in 5ml ethanol is refluxed over a water bath in a magnetic stirrer with $CuCl_2.2H_2O$ (0.005mol, 0.85g) in 5ml ethanol for three hours at 60^oC. The reaction mixture was eroded with enormous quantity of ice-cold water. Brown coloured precipitate was formed. It is filtered and dried with vacuum. The consumption of reactant molecules wereidentified by TLC technique. The crude product was recrystallized in hot alcohol for additional purification purposes.

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Bis-(4-benzylidene-3-methyl-1H-pyrazol-5(4H)-one)-copper (II) chloride (1b)

Brown solid; mw: 358.71; mp: 246°C; UV λ^{MeOH}_{max} nm (abs): 236 (1.24), 274 (1.41);IR (cm^{-1}): 3317.02 (NH), 2982.07 (CH), 1709.53 (C=O), 1499.48 (C-N); Elemental analysis: Calculated. For $C_{10}H_{16}Cl_2CuN_4O_2$: C, 33.48; H, 4.50; N, 15.62; %. Found: C, 33.50; H, 4.49; N, 15.61; %.

Synthesis of Bis-(1,3-cyclohexanedione)-Copper (II) complex (1c).

The compounds 1,3-cyclohexanedione (0.01mol, 1.12) in 5ml ethanol is refluxed over a water bath in a magnetic stirrer with $CuCl_2.2H_2O$ (0.005mol, 0.85g) in 5ml ethanol for three hours at 60^oC. Then 30ml of 10% NaOH solution was added. Green coloured precipitate was formed. It is filtered and dried with vacuum. The consumption of reactant molecules were identified by TLC technique. The crude product was recrystallized in hot alcohol for additional purification purposes.

Bis-(1,3-cyclohexanedione)-copper (II) (1c)

Black solid; mw: 287.80; mp: >360°C; UV λ^{MeOH}_{max} nm (abs): 291 (4.00), 391 (2.60), 395 (2.42) and 664 (1.05);IR (cm^{-1}): 2102.55 (CH), 1639.52 (C=O), 1188.22 (C-O); Elemental analysis: Calculated. For $C_{12}H_{16}CuO_4$: C, 50.08; H, 5.60; %. Found: C, 50.07; H, 5.61; %.

Larvicidal activity

Larvicidal bio-assay procedure from the previous literature [28]. The commercial pesticide *Permethrin*was used as a standard. The LD_{50}values were assessedwith probit exploration and the fallouts were examinedwith the SPSS v16 software.

Larval growth inhibition and regulation of *Culexquin quefasciatus*was determined by the water immersion method [29].

Antifeedant activity

Marine fishes (1.5–2.0 cm) *Oreochromismossambicus* were used for antifeedant activity evaluation [30].

Results and Discussion

Chemistry

The complex **1a**was prepared conferring to the synthesis pathwaydemonstrated in scheme 1. Complex **1b** was prepared conferring to the synthesis pathway demonstrated in scheme 2. The complex **1c** was prepared conferring to the synthesis pathway demonstrated in scheme 3. Complex **1a** was synthesized by the condensation reaction with using N-aminoethylethanolamine reacted with $CuCl_2.2H_2O$ in ethanol medium (Scheme 1). The complex **1b** was synthesized by 3-methyl-1H-pyrazol-5(4H)-one reacted with $CuCl_2.2H_2O$ by condensation method (Scheme 2).

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The complex **1c** was synthesized by 1,3-cyclohexanedione reacted with $CuCl_2.2H_2O$ by condensation method (Scheme 3) The confirmation compounds with the help of UV and IR spectral data.

Scheme 1. One-pot two component synthesis of Bis-(N-aminoethylethanolamine)-Copper (II) chloride (1a).

Scheme 2. One-pot two component synthesis of Bis-(4-benzylidene-3-methyl-1H-pyrazol-5(4H)-one)-copper (II) chloride (1b).

Scheme 3. One-pot two component synthesis ofBis-(1,3-cyclohexanedione)-copper (II) (1c).

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Spectral results

UV-VIS profile of complex **1a**was deliberate at a wavelength range of 200 to 800 nm. Three major bands were noticed at 225, 253 and 591 nm with absorbance values of 0.65, 0.79 and 0.02 respectively (*Figure 1*).

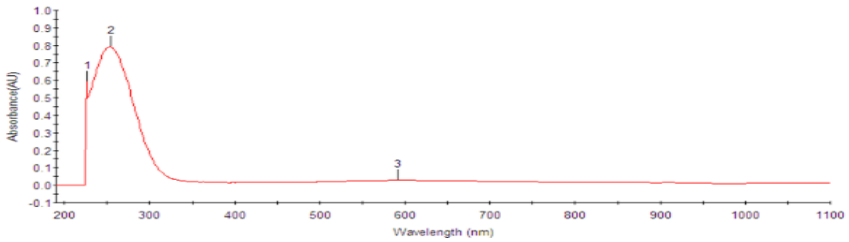

Figure 1. UV spectrum of complex **1a**.

FT-IR spectrum of complex **1a**(*Figure 2*) was executed to recognize the functional groups extant incomplex based on the peak values in the region of infrared radiation. The major bands were observed at V^{KBr} cm^{-1}: 3759.70, 3410.74, 2922.91, 1474.46, 1018.83, 745.22 and 670.80. The stretching bandat 3759.70 cm^{-1}specifies the absorption arising from Cu-OH. The stretching band at 3410.74 cm^{-1}signposts the absorption arising from Cu-NH. The stretching bandat 2922.91 cm^{-1}shows the absorption arising from C-H. The stretching bandat 1474.46 cm^{-1} is agrees to the presence of C-N moiety. The stretching bandat 1018.83 cm^{-1} confirms the C-O bond in the alcohol moiety. The bandat 745.22 cm^{-1}directs the bending vibration of aliphatic C-H bonds. The peak at 670.80 cm^{-1} corresponds to the disubstituted moiety in the aliphatic compound.

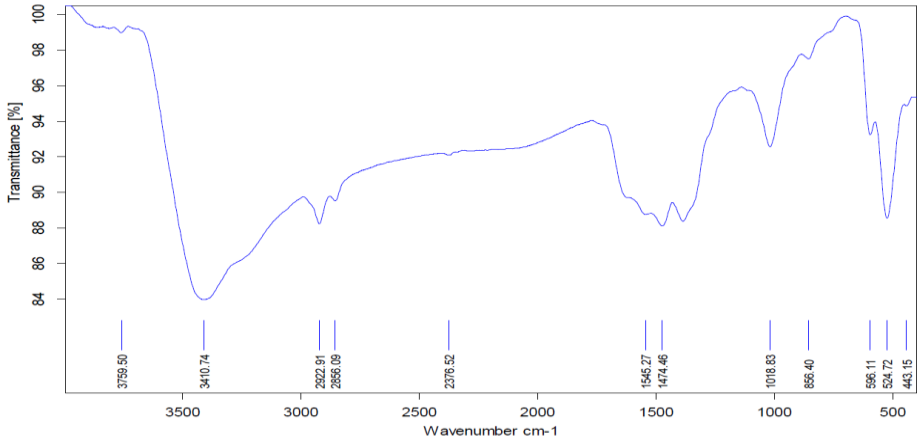

Figure 2. IR spectrum of complex **1a**.

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UV-VIS profile of complex **1b**was examined at a wavelength rangesbetween 200 to 800 nm. Two major bands were noticed at 236 and 274 nm with absorbance values of 1.24 and 1.41 respectively (*Figure 3*).

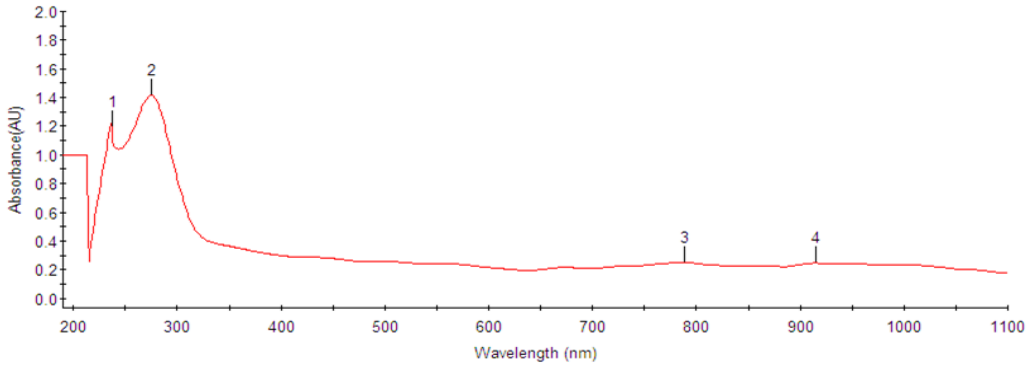

Figure 3. UV spectrum of complex **1b**.

FT-IR spectrum of complex **1b**(*Figure 4*) was did to detect the functional groups present in complex based on the peak values in the region of infrared radiation. The major bands were observed at V^{KBr} cm^{-1}: 3317.02, 2982.07, 1709.53, 1499.48, 745.22 and 670.80. The stretchingbandat 3317.02 cm^{-1} indicates the absorption arising from Cu-NH. The stretching bandat 2982.07 cm^{-1}designates the absorption arising from C-H. The stretching bandat 1709.53 cm^{-1} is corresponds to the presence of Cu-CO. The stretching bandat 1499.48 cm^{-1} is corresponds to the presence of C-N. The bandat 745.22 cm^{-1}specifies the bending vibration of aliphatic C-H bonds. The peak at 670.80 cm^{-1} corresponds to the disubstituted moiety in the aliphatic compound.

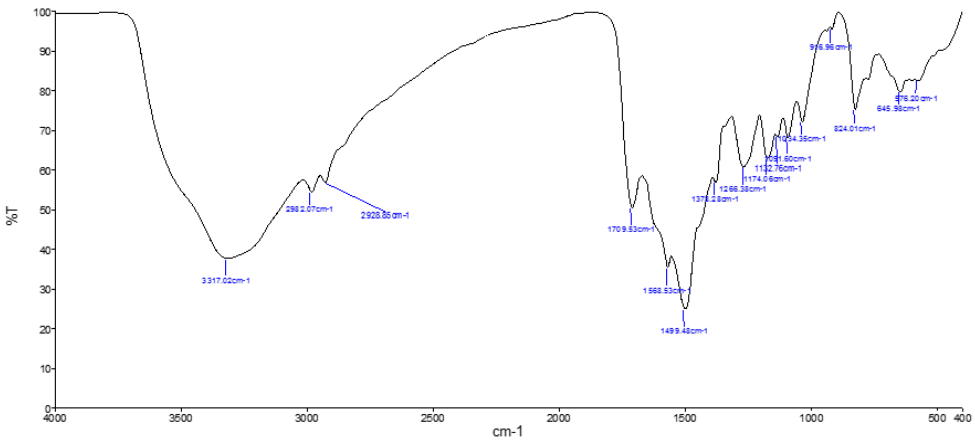

Figure 4. IR spectrum of complex **1b**.

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UV-VIS profile of complex **1c**was carriedout at a wavelength range of 200 to 800 nm. Four major bands were noticed at 291, 391, 395 and 664 nm with absorbance values of 4.00, 2.60, 2.42 and 1.05 respectively (*Figure 5*).

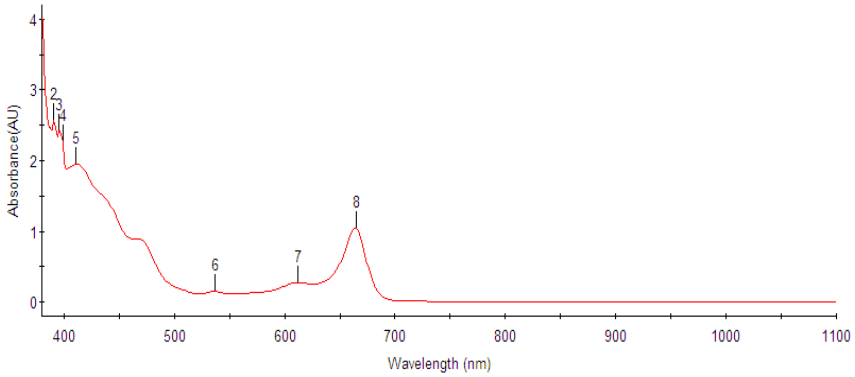

Figure 5. UV spectrum of complex **1c**.

FT-IR spectrum of complex **1c**(*Figure 6*) was achieved to findout the functional groups involved in complex formation based on the peak values in the region of infrared radiation. The major bands were observed at V^{KBr} cm^{-1}: 3572.80, 2102.55, 1639.52, 1188.22, 745.22 and 670.80. The stretching bandat 3572.80 cm^{-1} is resembles the presence of Cu-OH. The peak at 2102.55 cm^{-1} indicates the absorption arising from C-H stretching. The stretching bandat 1639.52 cm^{-1} is corresponds to the presence of Cu-CO. The stretching bandat 1188.22 cm^{-1} is corresponds to the presence of C-O group. The band at 745.22 cm^{-1}directs the bending vibration of aliphatic C-H bonds.The peak at 670.80 cm^{-1}relates to the disubstituted moiety in the aliphatic compound.

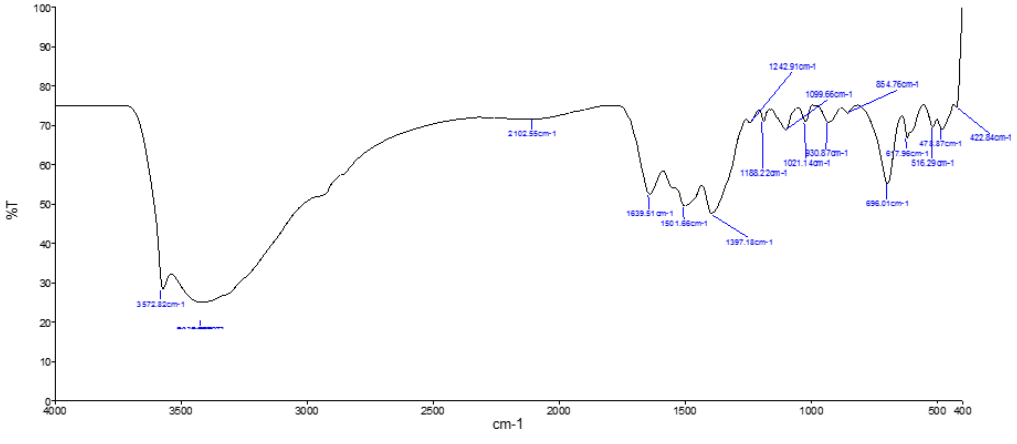

Figure 6. IR spectrum of complex **1c**.

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Magnetic Susceptibility Measurement

Table 1 shows the magnetic susceptibility of copper complexes measured at room temperature using Gouy's technique using $Hg[Co(SCN)_4]$ as a calibrant. The real magnetic moments were calculated using pascal's constants after smearing diamagnetic enhancements for the ligand components. At room temperature, the eff values of copper complexes ranged from 1.71 to 1.88 B.M. With octahedral geometry over the core metal ion, the magnetic susceptibilities of the complexes are reliable.

Table 1. Magnetic moment values of the copper (II) complexes **(1a – 1c**)

Complex	**Magnetic moment (B.M.)**
1a	1.84
1b	1.88
1c	1.71

Larvicidal activity

Complex **1b** has a higher LD_{50} value of 45.28 µg/ml against Culex quinquefasciatus than complexes **1a** and **1c**, which had LD_{50} values of 69.83 and 84.73 µg/ml, respectively. With LD_{50} values of 84.73 µg/ml, compound **1c** was the least potent against Culex quinquefasciatus among the produced complexes 1a–1c. In comparison to the positive control **Permethrin** with an LD_{50} of 60.03 µg/ml, compound **1b** was extremely active and complex **1a** was moderately active among the synthesized complexes **1a–1c**. Table 2 summarizes the results.

Table 2. Larvicidal activity of synthesized complexes **(1a – 1c**)

Comp.No.	**Mortality (%)Room temp Concentration(µg /mL)[a]**				**LD_{50} (µg /mL)**
	100	50	25	10	
1a	68± 0.67	40 ± 1.29	24± 1.78	12± 0.98	69.83
1b	80± 1.44	60± 1.30	40± 1.43	20± 1.29	45.28
1c	60± 1.64	30± 0.54	10± 0.34	0± 0.00	84.73
Positive control	-	-	-	-	60.03

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Negative control	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0

Positive control: Permethrin
Negative control:DMSO
[a]Value were the means of three replicates ± SD.

Antifeedant activity (Ichthyotoxicity activity)

Complex **1b** has a significant toxicity level when compared to complexes **1a** and **1c**. At 100 µg/ml, Complex **1a** caused 66 percent mortality in 24 hours. Toxicity was measured as a proportion of people dying within 24 hours. At 100 µg/ml, Complex **1b** caused 60% mortality in 24 hours. Table 3 summarizes the results. The complex **1a** was the most active of the synthesized complexes, with an LD_{50} of 69.57 µg/ml.

Table 3.Antifeedant activity of synthesized complexes **(1a – 1c**)

Comp.No.	**Mortality (%)Room temp Concentration(µg /mL)[a]**				**LD_{50} (µg /mL)**
	100	50	25	10	
1a	66±1.45	42±0.78	28±1.18	12±0.06	69.57
1b	66±2.12	41±1.34	22±1.73	10±1.47	71.89
1c	33±1.22	0±0.00	-	-	>100
Negative control	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± .0	0.0± 0.0

[a]Value were the means of three replicates ± SD.

Mosquito larval Growth inhibition activities.

The effects of complex **1b** after a 72-hour management on the weight increase of larvae and inhibitory rates were tracked and reported in Table 4 in accordance with the copper complexes guideline on growth, development, and metamorphosis. At 10 µg/ml, the pupal and adult phases, as well as the eclosion rate of the treated Culexquin quefasciatus, were assessed (Table 5). Complex **1b** reduced the development of larvae, with inhibitory rates of 41.36 percent. The effects of complex **1b** on the length of the pupal and adult phases were unclear, although eclosion rates were only 55 percent following complex **1b's** activity. Complex **1b** had excellent inhibitory capacity against Culexquin quefasciatus growth and development, according to the findings.

Table 4. The effect of complex **1b** on the growth of mosquito larvae

Comp.No	*Culexquin quefasciatus*

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	Weight (mg)		Weight gain (mg)	Inhibition (%)
	0 h	72 h		
1b	100.28	104.14	3.86	41.36
Control	100.06	106.65	6.58	-

Table 5. The effect of complex **1b** on the growth and development of mosquito larvae

Comp.No	*Culexquin quefasciatus*		
	Duration of pupae (h)	Duration of adult (h)	Rate of eclosion (%)
1b	68.1	23.1	55
Control	65.5	24.2	80

Conclusion

The present study, which concludes the effectiveness of Copper complexes having significant activity in larvicidal and antifeedant, bioassays. Complex **1b** showedremarkable activity against mosquito larvae compared with positive control and also less toxic in non-target aquatic species(antifeedant activity). Therefore, these complexes might be a probablebasis for emergingeconomically significant bioactive compounds, as well as biodegradable pesticides, and biopharmaceuticals.

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