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(Research Article)

Synthesis of Cd (II), Fe (III), Cu (II), and Cr (VI) complexes of Schiff bases and their antibacterial activities

Godwin Asukwo Ebong *, Atim Sunday Johnson, Idongesit Bassey Anweting, Helen Solomon Etuk and Victor Nkereuwem Mkpenie

Department of Chemistry, University of Uyo, Akwa Ibom State, Nigeria.

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Abstract

Schiff base and the metal derivatives have been utilized in numerous areas of the economy. Synthesis and antibacterial activities of Cd (II), Cr (VI), Cu (II), and Fe (III) complexes of Schiff bases were evaluated in this work. Complexes synthesized were Bis(1-phenyl-3-methyl-4-Phenyl acetyl 5-pyrazolone)Cadmium (II) ($Cd(HPMPP)_2$), Tris(1-phenyl-3-methyl-4-benzoyl-5-pyrazolone)Iron(III)($Fe(HPMBP)_3$), Bis(1-phenyl-3-methyl-4-phenylacetyl-5-pyrazolone)Copper (II) ($Cu(HPMPP)_2$), Hexakis(1-phenyl-3-methyl-4-palmitoyl-5-pyrazolone)Chromium (VI) ($Cr(HPMPP)_6$), and Tris(1-phenyl-3-methyl-4- palmitoyl-5-pyrazolone)Iron (III) ($Fe(HPMPP)_3$). The physical state, colour, and melting point of these complexes were determined using appropriate analytical techniques. Results showed that all the complexes were crystalline in nature; their colours were variable, while their melting points were sharp. The solubility of these complexes in deionized water, acetone, methanol, and ethanol was also carried out. The outcome revealed that all the metal complexes were insoluble in deionized water, $Cr(HPMPP)_6$ was soluble in acetone, methanol, and ethanol. However, the solubility of other metal complexes in the organic solvents used was variable. The antibacterial activities of these metal complexes at different concentrations were also tested against distilled water, *E. coli, S. aureus, B. subtillus, and S. typhi*. The results showed that, antimicrobial activity of these complexes against distilled water was negative whereas, the bacterial growth of all the bacteria was inhibited by the complexes though at different rates. The inhibition rate of microorganisms was inversely proportional to the concentration of the complexes. The antibacterial activities of $Cd(HPMPP)_2$ and $Cr(HPMPP)_6$ were outstanding against the growth of all the bacteria. Thus, a proper processing of these complexes might result in excellent antibacterial drugs. However, more studies on the mode of action of these complexes against microorganisms and their toxicity should be done in order to establish their potentials for pharmaceutical applications.

Keywords: Metal complexes; Antimicrobial activity; Metal complexes; Antimicrobial activity; Schiff base; Inhibitory effect

1. Introduction

The discovery of Schiff base by a German chemist Hugo Schiff in 1864 has attracted several researches on the synthesis of metal complexes of Schiff bases [1]. Metal complexes of Schiff bases have been utilized in various ways and their imine (-RC=N-) and azomethine (>C=N–) groups are the vital functional groups necessary for their applications. Metals are toxic at concentrations higher than their recommended levels and their toxicities are mostly noticed in highly contaminated environments [2, 3]. However, a combination of metals with Schiff bases can result in complexes with effective antimicrobial properties. Metal complexes of Schiff bases have been reported to have analgesic, antipyretic, anti-inflammatory, and antifungal properties [4-6]. Reports have also shown that, these complexes have antimalaria, antiviral, and antibacterial properties [7-9]. It has also been reported that, metal complexes of Schiff bases have been utilized for the control of nematode, insects as well as plant growth regulation [10-12]. They have antileukaemia,

*Corresponding author: Godwin Asukwo Ebong

antioxidant, anti cancer, and anti-HIV properties [13-15]. These complexes are used effectively as corrosion inhibitors, in analytical researches, and dye industry [16-18].

In this work, Cd (II), Fe (III), Cu (II), and Cr (VI) complexes of Schiff bases were synthesized and tested for their antibacterial effects on *E. coli, S. aureus, B. subtillus, and S. typhi*. Studies revealed that *E. coli* can cause pneumonia, urinary tract infection, diarrhea, fever, nausea, vomiting, abdominal pains and meningitis in human body [19, 20]. *S. aureus* causes infections of the skin tissues, bloodstream, bone and joint [21]. The bacteria (*S. aureus*) are mostly witnessed in patients with diabetes mellitus, immune deficiency, cardiovascular, and granulocytic problems [22]. Exposure of human to *B. subtilis* could cause pneumonia, bacteremia, septicemia, and endocarditis [23]. Reports have shown that, health hazards associated with the exposure to *S. Typhi* include fatigue, nausea, abdominal pain, extended high fever, and diarrhea [24, 25]. Consequently, extensive studies on antibacterial properties of metal complexes of Schiff bases are necessary for the control and subsequent extermination of diseases related to these bacteria and their symptoms.

2. Materials and methods

2.1. Synthesis of metal complexes

During this research, the respective ligands of the complexes were synthesized however; based on literature, metal complexes of Schiff bases are more efficient as antimicrobial agents than their ligands [26, 27]. Thus, emphasis in this study was on the metal complexes rather than their ligands as previously reported by Laiq and Shahid, [28].

Bis(1-phenyl-3-methyl-4-Phenyl acetyl 5-pyrazolone) Cadmium (II) was synthesized by dissolving 2 mmol of $CdCl_2$ in 10 ml deionized water and mixed drop-wisely with stirring to a test tube containing 1 mmolof already synthesized 1-phenyl-3-methyl-4-Phenyl acetyl-5-pyrazolone in 10 ml ethanol. The pH of the mixture was maintained by the addition of ammonium hydroxide and the mixture was kept until white crystals were formed. These crystals were filtered off, recrystallized in ethanol and air dried for five days [29].

The synthesis of tris(1-phenyl-3-methyl-4-benzoyl-5-pyrazolone) Iron (III) was done by dissolving iron (III) sulphate in 100 ml warm water and adding dropwisely with stirring to a boiling solution of a freshly prepared 2.5 mmol 1-phenyl-3-methyl-4-benzoyl-5-pyrazolone in 200 ml ethanol. The resulting precipitate was filtered, recrystallized in chloroform, and air dried for five days [30].

Bis(1-phenyl-3-methyl-4-phenylacetyl-5-pyrazolone) Copper (II) was synthesized by dissolving 2 mmol copper (II) sulphate in 10 ml deionized water and adding with stirring to a boiling solution of 1 mmol of freshly prepared 1-phenyl-3-methyl-4-phenylacetyl-5-pyrazolone in 10 ml ethanol. The mixture was allowed to stand until crystals were formed. These crystals were filtered off and recrystallized in ethanol [31].

Table 1 Metal Complexes and their respective symbols

	Metal Complex	**Symbol**
i.	Bis(1-phenyl-3-methyl-4-Phenyl acetyl 5-pyrazolone) Cadmium (II)	$Cd(HPMPP)_2$
ii.	Tris(1-phenyl-3-methyl-4- benzoyl-5-pyrazolone) Iron (III)	$Fe(HPMBP)_3$
iii.	Bis(1-phenyl-3-methyl-4-phenylacetyl-5-pyrazolone) Copper (II)	$Cu(HPMPP)_2$
iv.	Hexakis(1-phenyl-3-methyl-4-palmitoyl-5-pyrazolone) Chromium (VI)	$Cr(HPMPP)_6$
v	Tris(1-phenyl-3-methyl-4- palmitoyl-5-pyrazolone) Iron (III)	$Fe(HPMPP)_3$

The synthesis of hexakis(1-phenyl-3-methyl-4-palmitoyl-5-pyrazolone) Chromium (VI) was carried out by dissolving 0.588 g of potassium dichromate (VI) in 50 ml deionized water and mixed with freshly prepared 0.304 g 1-phenyl-3-methyl-4-palmitoyl-5-pyrazolone in 50 ml ethanol.The mixture was allowed to stand till crystals were formed. These crystals were filtered off, recrystallized in ethanol, and air dried for five days [28].

Synthesis of tris(1-phenyl-3-methyl-4- palmitoyl-5-pyrazolone) Iron (III) was done by reacting 2 mmol iron (III) sulphate in 100 ml warm water with a boiling solution of 2.5 mmol of already prepared 1-phenyl-3-methyl-4- palmitoyl-5-pyrazolone in 200 ml ethanol. The pH of the mixture was maintained by the addition of ammonium hydroxide. The

mixture was kept until reddish crystals were formed. The crystals were filtered off, washed with deionized water, and recrystallized in ethanol [30]. All pure crystals obtained were stored in dry clean containers and kept in a dessicator for analyses. In this research, metal complexes of Schiff bases synthesized and their symbols are indicated in Table 1 above.

2.2. Solubility test

The complexes obtained were dissolved in deionized water, acetone, methanol, and ethanol to ascertain their solubilities in these solvents.

2.3. Melting point determination

Melting point of the metal complexes synthesized was determined using Gallenkamp melting point equipment with digital thermometer model MPD 350.BM.3.5. A small quantity of each of the metal complex was put in a capillary tube with one end closed and inserted into the melting point apparatus connected to a power source. The initial and final melting points of the complex were recorded from the screen

2.4. Antibacterial activity test

The antimicrobial susceptibility of the isolates to the extract was determined using the Kirby-Bauer Method [32, 33]. The different concentrations (0.2 mg/L, 0.4 mg/L, and 0.6 mg/L) of the extract were impregnated unto paper disk of 4 mm diameter and placed in a Mueller Hintor Agar plate seeded with *Escherichia coli, Staphylococcus aureus, Bacillus subtillus, and Salmonella typhi* using sterile forceps. The plates were then incubated for 18-24 hours and the diameter of the zones of inhibition around the disc were measured and recorded to nearest mm [34, 35]. In this study, deionised water was used as the Control as reported by Matar *et al*. [36] and Yousif *et al*. [37].

3. Results and discussion

Table 2 Physical properties of the metal complexes

		Physical Properties			**Solubility Test**			
		Physical state	**Colour**	**Melting point**	**Deionized water**	**Acetone**	**Methanol**	**Ethanol**
i.	$Cd(HPMPP)_2$	Crystalline	White	263.1 – 264.2	IS	IS	IS	S
ii.	$Fe(HPMBP)_3$	Crystalline	Milky	259.4 – 261.2	IS	S	S	IS
iii.	$Cu(HPMPP)_2$	Crystalline	Green	268.8 – 270.2	IS	IS	S	S
iv.	$Cr(HPMPP)_6$	Crystalline	Orange	268.0 – 272.2	IS	S	S	S
v	$Fe(HPMPP)_3$	Crystalline	Red	261.1 – 263.3	IS	S	S	IS

S = Soluble; IS = Insoluble

3.1. Physical characteristics of the metal complexes

The results in Table 2 indicate that, all the metal complexes synthesized were crystalline in nature, $Cd(HPMPP)_2$, $Fe(HPMBP)_3$, $Cu(HPMPP)_2$, $Cr(HPMPP)_6$, and $Fe(HPMPP)_3$ were white, wine, green, orange, and reddish in colour, respectively. Obviously, the oxidation state of the metals might have influenced the colours exhibited by their complexes [38]. The melting/decomposition points (°C) of the complexes varied for $Cd(HPMPP)_2$, $Fe(HPMBP)_3$, $Cu(HPMPP)_2$, $Cr(HPMPP)_6$, and $Fe(HPMPP)_3$ as follows: 263.1 – 264.2, 259.4 – 261.2, 268.8 – 270.2, 268.0 – 272.2, and 261.1 - 263.3, respectively. This shows that the melting points of the complexes were high and sharp. This could be attributed to complexation and the pure nature of the complexes [39]. Table 2 shows that, all the metal complexes were insoluble in water as previously reported by Iorungwa *et al*. [40].According to Karmakar *et al*. [41], the solubility of metal complex in a solvent depends mainly on the nature of the solvent, ligand, and the central metal. Thus, the solubility of the complexes varied from one solvent to another as indicated below. $Cd(HPMPP)_2$ was insoluble in acetone and methanol, but soluble in ethanol whereas $Fe(HPMBP)_3$ was soluble in acetone and methanol, but insoluble in ethanol. $Cu(HPMPP)_2$ was insoluble in acetone but soluble in both methanol and ethanol. $Cr(HPMPP)_6$ was soluble in acetone, methanol, and ethanol while $Fe(HPMPP)_3$ was insoluble in ethanol but soluble in acetone and methanol.

Table 3 Results of inhibitory effects (mm) of the metal complexes for 0.2, 0.4, and 0.6 mg/Lconcentrations

	$Cd(HPMPP)_2$			**$Fe(HPMBP)_3$**			**$Cu(HPMPP)_2$**			**$Cr(HPMPP)_6$**			**$Fe(HPMPP)_3$**		
	0.2	**0.4**	**0.6**	**0.2**	**0.4**	**0.6**	**0.2**	**0.4**	**0.6**	**0.2**	**0.4**	**0.6**	**0.2**	**0.4**	**0.6**
Distilled water	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
E. coli	21	19	16	8	6	4	9	7	4	20	17	15	8	6	6
S. aureus	20	17	15	3	3	1	8	5	4	9	7	4	3	2	1
B. subtillus	22	18	16	5	4	3	7	6	4	16	13	10	5	5	3
S. typhi	12	10	8	2	1	1	8	6	5	9	7	5	2	1	1

3.2. Inhibitory activities of metal complexes

Table 3 indicates the results for antimicrobial activities of metal complexes at 0.2, 0.4, and 0.6 mg/L concentrations. The inhibitory effects of $Cd(HPMPP)_2$ on all the microorganisms tested indicated the concentration of the metal complex was inversely proportional to the inhibition zones of the organisms. The inhibition zones of *Escherichia coli, Staphylococcus aureus, Bacillus subtillus, and Salmonella typhi* due to treatment with $Cd(HPMPP)_2$ were the highest compared to other metal complexes synthesized (Table 3).The antibacterial effects of metal complexes on *Escherichia coli, Staphylococcus aureus, Bacillus subtillus, and Salmonella typhi* decreasedwith increase in the concentrations of the complexes. The lowest inhibition zone (1 mm) for each of the bacteria was recorded at a metal complex concentration of 0.6 mg/L. However, the highest inhibition zone for each of the test microorganism was obtained at a metal complex concentration of 0.2 mg/L (Table 3). The inhibitory effects of $Cr(HPMPP)_6$ against all the microorganisms were the next after $Cd(HPMPP)_2$. Generally, the inhibitory effects of metal complexes synthesized on all the microorganisms followed a decreasing order of $Cd(HPMPP)_2$> $Cr(HPMPP)_6$> $Cu(HPMPP)_2$, $Fe(HPMPP)_3$ = $Fe(HPMBP)_3$. Based on the results obtained, if $Cd(HPMPP)_2$ and $Cr(HPMPP)_6$ are properly processed it could be used for the treatment of diseases associated with *E. coli, S. aureus, B. subtillus, and S. typhi.* However, $Cd(HPMPP)_2$ will give a better efficacy against these microorganisms than $Cr(HPMPP)_6$. This similar to the results obtained by Pavel *et al.* [42] in their study on antimicrobial effects on soil microorganisms.It could as well be deduced from the results that, the toxicity of the metal may influence the inhibitory effects of metal complexes against microorganisms [43-45]. The inhibition zone for the Control (Distilled water) was zero for all the metal complexes and the various concentrations [46]. This confirms the antibacterial potency of the metal complexes of Schiff bases synthesized.

4. Conclusion

Results obtained from this research have shown that, the metal complexes synthesized were pure as indicated by their sharp melting points. The study has also revealed that, all the complexes synthesized have potency against the activities of *E. coli, S. aureus, B. subtillus, and S. typhi* as disease-causing agents. However, the efficacy of Bis(1-phenyl-3-methyl-4-Phenyl acetyl 5-pyrazolone) Cadmium (II) and Hexakis(1-phenyl-3-methyl-4-palmitoyl-5-pyrazolone) Chromium (VI) against the activities of these microorganisms were highly commendable. Consequently, if these complexes are properly harnessed and utilized as drugs against diseases caused by *E. coli, S. aureus, B. subtillus, and S. typhi*, the outcome could be amazing. Thus, the processing and utilization of Bis(1-phenyl-3-methyl-4-Phenyl acetyl 5-pyrazolone) Cadmium (II) and Hexakis(1-phenyl-3-methyl-4-palmitoyl-5-pyrazolone) Chromium (VI) as antimicrobial drugs by pharmaceutical Companies is highly recommended.

Compliance with ethical standards

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Disclosure of conflict of interest

No conflict of interest to be disclosed.

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