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SYNTHESIS AND ANTIBACTERIAL STUDIES OF MIXED METRONIDAZOLE- VITAMIN C METAL COMPLEXES

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Abstract

The reaction of metronidazole and vitamin C with Co(II) and Zn(II) have yielded some novel complexes. The novel complexes were found to be stable.

The antibacterial studies was investigated against *Eschericia Coli*, *Bacillus Subtilis* and *Staphylococcus aureus*. The result showed that all the novel mixed Complexes showed higher activity than the original metronidazole and vitamin C

KEYWORDS: Antibacterial, metronidazole, vitamin C, complexes

Introduction

The development of more effective chemotherapeutic agent has been the main goals of coordination chemists over the years it has been discovered that metal complexes have enormous impact in medicine (Ogunniran et al, 2008)

The use of metal complexes capable of enhancing biological activity has become a vibrant and growing area of research among inorganic chemists and biologists over the last few decades. Some metal complexes have been found to have antimicrobial and antiviral properties and could be effective against diseases (Behren et al, 1996).

As part of our continuation on the study of metal complexes, we intend to study mixed metal complexes of vitamin C with metronidazole. It is hoped that the mixed complexes will be more bacterial active than the metronidazole complexes and vitamin c metal complexes.

Vitamin C (L-ascorbic acid) is a water-soluble antioxidant. It has a great reducing potential and reacts with many reactive oxygen and nitrogen species

in -vitro. In addition to food industry, vitamin C is extensively used in a number of cosmetic products to protect the skin from environmental damages and photoaging (Hak. H. Kang and Seong-Geun Oh (2003).

However, one disadvantage of vitamin C is its chemical instability in aqueous solution where it becomes quickly oxidized and denatured.

Although, Callaghan. (1983) reported the synthesis of platinum and copper complexes of Metronidazole and 2- methyl-5-nitrobenzimidazole. In 2007, Obaleye and Lawal reported the synthesis of Co (II), Ni (II) and Fe (III) complexes of metronidazole, it was reported that the complexes were found to have higher antifungal activities than the original metronidazole.

Also, some metal complexes of vitamin C have been synthesized as reported by (Obaleye & Orjiekwe, 1992).

To overcome the problem of non-bacterial activity of ascorbic acid metal complexes, we decided to prepare some mixed complexes of ascorbic acid with metronidazole.

Thus, in this study, we reported the synthesis and antibacterial studies of mixed metronidazole-vitamin C complexes.

Materials and Methods

All the reagents were of standard analytical grade and were used as supplied, without further purification.

Metronidazole and vitamin C were obtained from Sam Pharmaceutical Limited, Ilorin, Kwara State, Nigeria.

The nutrient agar, pure culture of *E-Coli*, *Bacillus Subtilis* and *Staphylococcus* were obtained from the Department of Microbiology, University of Ilorin.

Synthesis of metronidazole metal complexes

The procedure employed by Obaleye and Lawal, 2007 was used. The complexes were prepared by adding an aqueous solution of the hydrated metal chloride (2.5mmol) to an aqueous solution of metronidazole (5mmol, 0.8558g). The mixture was refluxed for 2 hours and left for 3 days before complexation. The precipitated complex was removed by filtration and washed with distilled water and methanol, it was dried in a dessicator.

Synthesis of vitamin C-metal complexes

An aqueous solution of the metal salt (2.5mmol) in distilled water (10ml) was added to an aqueous solution of the vitamin C (5mml, 0.8803g). The mixture was refluxed for 3hours and left for four days before complexation. The precipitated complex was removed by filtration, followed by washing in distilled water and dried in a dessicator.

Synthesis of mixed metronidazole-vitamin C complexes

0.855g (5mmol) of metronidazoles in 10ml of distilled water was added to 0.8803g (5mmol) of vitamin C in 20ml of methanol, the was colour change which vary with respect to the metal salt used. 2.5mmol of the metal salt were added to the mixture. The mixture was refluxed for 3 hours and left two weeks before complexation. The precipitated complex was removed by filtration, washed with distilled water and methanol, dried in a dessicator.

Antibacterial studies

The antibacterial studies of the compounds was assayed against three bacteria: *Escherichia Coli*, *Bacillus Subtillis* and *Staphylococcus auereus*.

The antibacterial studies of the compound was determined as reported by Abd-El-wafa *et al*, 1987 and Obaleye, *et al*, 1995).

The antibacterial activity was determined on the seeded nutrient agar on which 0.9cm diameter were punch. Different concentrations (50ppm and 100ppm) of sterile filtered solutions of the ligands and the complexes were made using distilled water as solvent, 0.1ml of each concentration was applied into the wells and incubated at 37°C for 25 hours.

The average zone of inhibition in millimeter was determined from the readings taken in triplicate. Distilled water was used as a control.

Table 1: Results of some physical properties of the ligands and the complexes

Compound	Colour	Melting point (°C)	Molar conductance Ω^{-1}
Metronidazole	White creamy	158 – 160	2.10×10^{-7}
Vitamin C	Whitish	190	8.80×10^{-4}
Cu(met) ₂ Cl ₂	Cream	152 – 154	2.34×10^{-6}
Zn(met) ₂ Cl ₂	Whitish	148 – 150	3.00×10^{-6}
Cu(vitc) ₂	Deep blue	176 – 178	5.2×10^{-5}
Zn(vitc) ₂	Whitish	170 – 172	2.30×10^{-5}
Cu(met) (vitc)Cl ₂	Deep green	>300	5.10×10^{-6}
Zn(met) (vitc)Cl ₂	Pale yellow	>300	3.60×10^{-6}

Table 2: Selected IR spectra Assignment of Metronidazole, vitamin C and their mixed complexes

Metronidazole (cm ⁻¹)	Vitamin C (cm ⁻¹)	Cu(Met)(Vit C)Cl ₂ (cm ⁻¹)	Zn(Met)(Vit C)Cl ₂ (cm ⁻¹)	Tentative Assignment
3780 (s,b) 3707(s)	3874(w) 3742(w) 3519(s) 3188(s)	3720(s)	3652(s)	O-H _{str}
1570(s) 1300(s)	-	1527(w)	1541(w)	N=O _{str}
1129(m)	-	1210(m)	1095(w)	C-N _{str}
-	1763(s)	1720(w)	1714(m)	C=O _{str}
-	1335(s)	1274(w)	1288(w)	O-H _{def}
-	-	513(w)	506(w)	M-OH

Table 3: UV/Visible spectra assignment of metronidazole, vitamin C and their mixed complexes

Ligand / Compound	Wavelength (nm)	Assignment
Metronidazole	314	$\Pi \rightarrow \Pi^*$
	262	$n - \Pi^*$
	227	$n - \Pi^*$
	198	$n - \sigma^*$
Vitamin C	254	$\Pi \rightarrow \Pi^*$
Cu(Met)(Vit C) Cl ₂	270	$\Pi \rightarrow \Pi^*$
	345	$d \rightarrow d^*$
Zn(Met)(Vit C) Cl ₂	282	$\Pi \rightarrow \Pi^*$
	366	$d \rightarrow d$

The results of the IR spectra of the ligands were compared with those of their mixed complexes

In the mixed complexes, metronidazole coordinate through the oxygen of the alcoholic group and the nitrogen i mine group.

The result of IR spectrum of vital..... supports that vitamin C binds to the metal ion through the oxygen of the carbonyl and that of C-2 hydroxyl groups. (Williams, 1980).

The UV/Visible spectral of the ligands were compared with those of its mixed complexes, the bands in the ligands have been shifted to higher wavelengths in the mixed complexes due to complexation (Orgel (1985).

Table 4: Antibacterial studies of the ligand and their complexes showing the zone of inhibition against the organisms.

Concentration	Compound	<i>Escherichia coli</i>	<i>Bacillus subtilis</i>	<i>Staphylococcus</i>
50ppm	Metronidazole	12±2.01	14±1.80	19±1.32
	Cu(met) ₂ Cl ₂	18±2.43	16±1.60	23±1.05
	Zn(met) ₂ Cl ₂	14±2.54	18±1.46	21±1.23
50ppm	Cu(met) (vitc) ₂ Cl ₂	22±2.60	27±1.18	26±2.02
	Zn(met) (vitc) ₂ Cl ₂	24±1.86	30±2.02	28±2.04
100ppm	Metronidazole	20±1.20	18±1.50	16±1.35
	Cu(met) ₂ Cl ₂	23±1.24	22±1.11	18±1.38
	Zn(met) ₂ Cl ₂	25±1.27	23±1.16	17±1.20
100ppm	Cu(met) (vitc) ₂ Cl ₂	32±2.01	24±1.74	36±2.01
	Zn(met) (vitc) ₂ Cl ₂	31±2.10	26±1.86	34±2.05

Values are mean of 3 replicates ± SD

All the complexes synthesized are coloured and very stable. The molar conductance data in methanol and distilled water indicate non-electrolytic behaviour in these solvents. The melting point of the mixed complexes compared to their respective ligands confirmed purity of the compounds.

Both metronidazole and vitamin C act as bidentate ligands in their mode of coordination with the metal ions. The results of the physical property of the ligands and the complexes are presented in Table 1.

The result of the antibacterial studies are presented in Table 4. The result showed that the mixed metronidazole – vitamin C Complexes possess higher inhibitory activity against all the three bacterial species at 100ppm concentration than 50ppm concentration (Rudziński *et al*, 1982).

The result of antibacterial studies of vitamin C metal complexes showed that all the metal complexes possess no activity against the raised bacterial species.

Conclusion

The novel mixed metronidazole – vitamin C Complexes were found to be very stable. The result of the antibacterial studies showed that all the novel mixed complexes showed higher activity compared to the metronidazole Complexes.

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