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EVALUATION OF ANTIVIRAL POTENTIAL AND PHARMACOKINETIC PROPERTIES OF OXAZOLIDINONE METAL COMPLEXES AGAINST SARS-COV-2

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Abstract

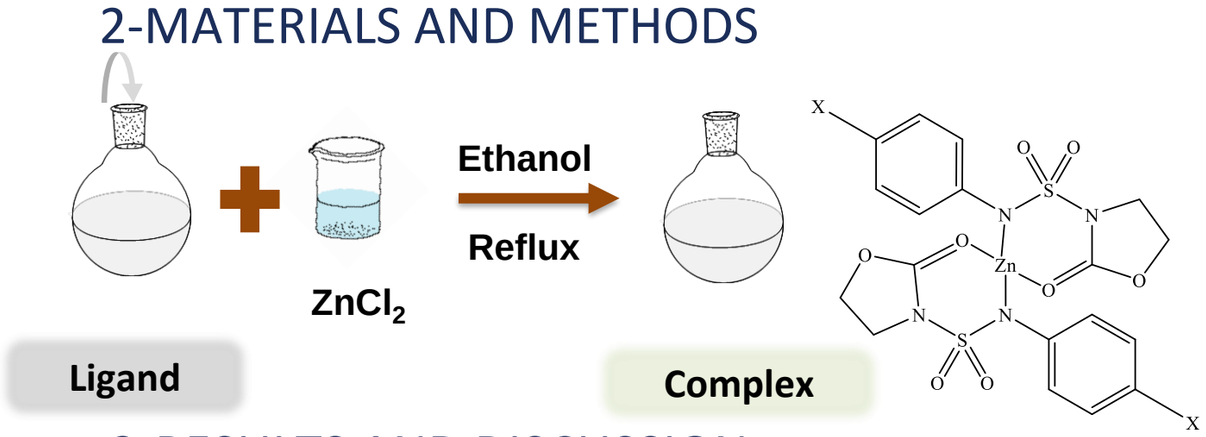
The metal complexes with oxazolidinone derivatives were synthesized and characterized using elemental analysis, molar conductivity, ICP emission, FT-IR, ^{1}H NMR, EPR, UV-Visible, and thermal analysis (TGA/DTG). In order to determine the antiviral and potential of oxazolidinone ligands and their metal complexes, an *in silico* study using molecular docking was carried out. In addition, the pharmacokinetic properties of the synthesized metal complexes were realized using ADMET study. The molecular docking simulation was realized to elucidate binding interactions between the compounds and protein of selected strain.

Mots-clés : Antiviral activity, SARS-Cov-2, Oxazolidinones, metal complexes, Molecular docking.

1-INTRODUCTION

The threat of infection is constantly increasing causing various diseases [1]. In this context, an urgent need for new active products has been established to act on various pathogenic agents. Oxazolidinones are recognized for their significant biological activity and are commonly utilized in medicine for their antibacterial, antifungal, antiviral, and anticancer properties For these reasons, oxazolidinone derivatives are good candidates for complexation with transition metals to enhance their biological potential [2], [3].

2-MATERIALS AND METHODS



3-RESULTS AND DISCUSSION

Table 1. Analytical and physical data of zinc complexes.

Compound	Exp (Calcd) (%) C	H	N	M	Melting point (°C)	Color	Yield (%)	Λ_{DMSO} (Ω^{-1} cm^2 mol^{-1})
$[Zn(L^1)_2]\cdot 0.5H_2O$	36.89 (37.03)	2.98 (3.01)	9.74 (9.60)	11.03 (10.86)	250	White	26	16.1
$[Zn(L^2)_2]$	36.09 (36.18)	2.68 (2.88)	8.73 (8.88)	10.44 (10.36)	260	Bright white	51	36.8
$[Zn(L^3)_2]\cdot 0.5H_2O$	30.54 (30.64)	2.02 (2.29)	7.85 (7.94)	9.32 (9.27)	250	White	62	43.0
$[Zn(L^4)_2]$	26.97 (27.04)	1.98 (2.02)	6.91 (7.01)	8.07 (8.18)	242	Beige	76	36.9

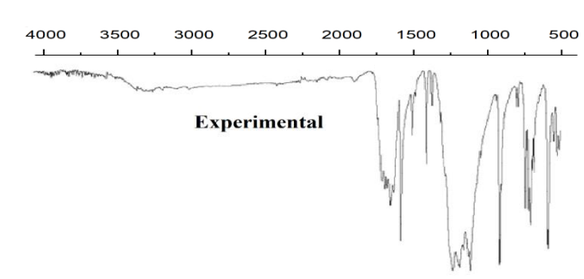


Figure 1. Experimental and theoretical infrared spectra of ZnL^4 complex.

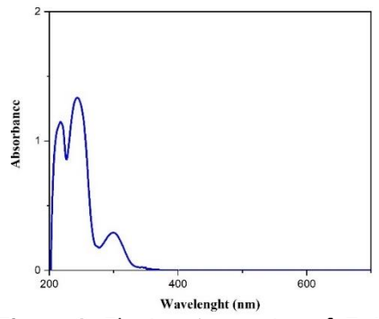


Figure 2. Electronic spectra of ZnL^3 (b).

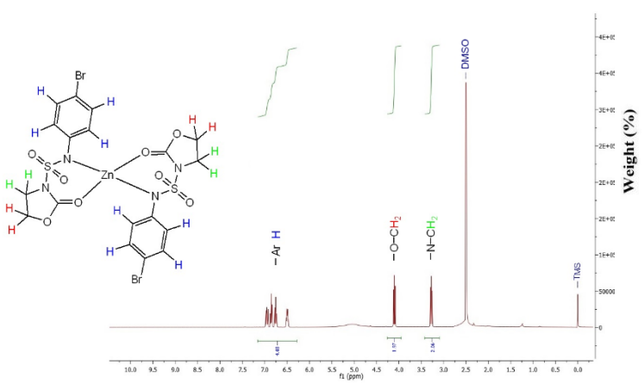


Figure 3. ^{1}H NMR spectra of ZnL^1.

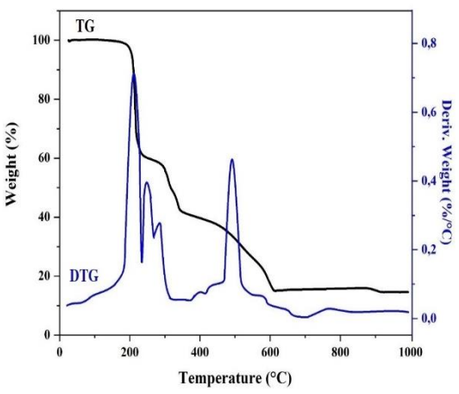


Figure 4. TG/DTG curves of $[Zn(L^4)_2]$.

Table 2. Binding energy intervals (kcal mol^{-1}) of the first 10 most stable states of Cible@compound.

Cible@ compound	Binding energy intervals	RMSD
$SP@HL^1$	-5.9 to -5.2	0.00 to 4.55
$SP@HL^2$	-5.6 to -4.9	0.00 to 3.46
$SP@HL^3$	-6.0 to -5.2	0.00 to 5.60
$SP@HL^4$	-5.4 to -4.6	0.00 to 8.57
$SP@ZnL^1$	-8.4 to -6.6	0.00 to 3.60
$SP@ZnL^2$	-7.9 to -6.3	0.00 to 3.89
$SP@Zn\text{-}L^3$	-6.0 to -5.4	0.00 to 3.92
$SP@Zn\text{-}L^4$	-6.3 to -5.5	0.00 to 4.66

Table 3. Predicted physicochemical and pharmacokinetic properties of the studied compounds.

Compound	BBB	GIA	CaCo2	Molecular weight (g mol^{-1})	TPSA (Å^2)	HBD	HBA	Rotatable bonds	LogP
HL1	0.7783+	0.8374+	0.6090-	260.24	84.09	1	5	3	1.01
HL2	0.6969+	0.8694+	0.6119-	276.70	84.09	1	4	3	1.17
HL3	0.7331+	0.8199+	0.6118-	321.15	84.09	1	4	3	1.28
HL4	0.7180+	0.5500+	0.6113-	368.15	84.09	1	4	3	1.37
ZnL^1	0.6931+	0.9947+	0.5968-	583.85	150.60	0	10	2	0.48
ZnL^2	0.6274+	0.9948+	0.5963-	616.76	150.60	0	8	2	0.86
ZnL^3	0.6499+	0.9925+	0.5964-	705.66	150.60	0	8	2	0.99
ZnL^4	0.6686+	0.9576+	0.6234-	801.68	134	0	10	2	0.99
SMX	0.9382+	1.000+	0.5346-	253.28	106.60	2	4	3	0.90
Linezolid	0.9363+	1.000+	0.8866+	337.35	71.11	1	5	5	1.23

4-CONCLUSION

The *in silico* antiviral evaluation was realized against SARS-Cov-2 protein and convincing results were obtained suggesting good antiviral potential for the ligands and their complexes. The results show that the compounds enter in the protein cavity and they are stabilized by hydrogen bonds and hydrophobic interactions. Moreover, the metal complexes showed a biological properties better than the free ligands, which indicate that the presence of metal ion enhance the biological potential. ADMET study and drug likeness show that the compound could be better absorbed from the intestinal tract upon oral administration and can penetrate through the Blood-Brain Barrier (BBB).

In conclusion, the synthesized oxazolidinone ligands and their metal complexes are candidates for pharmaceutical application as antiviral drugs.

Bibliographic references

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