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Synthesis, Characterization Antimicrobial Activities Studies Of Mixed-Ligand Complexes Of Curcumin And Anthranilic Acid With Bivalent Metals Chlorides.

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ABSTRACT

Mixed metal ligand complexes is reported with curcumin (CUM) as a primary ligand and Anthranilic acid (Anth) as secondary ligand. The structures of these complexes are confirmed by using FT-IR and UV-electronic spectroscopies, magnetic moments, melting points, molar conductivity measurements and the metal% analysis revealed that the complexes analyze indicates a six coordinated as $[M(CUM)(Anth)_2]$, M=Mn(II), Co(II), Ni(II), Cu(II), Zn(II), Cd(II), Hg(II). In-vitro antimicrobial studies on (Curcumin and Anthranilic acid) ligands and mixed metal ligand complexes against ((Bacillus subtilis (G+), Esherichia Coli (G-) and as well as antifungal activities against Candida albicans by measuring the zone of inhibition in mm.

Keywords: Curcumin, Anthranilic acid, antimicrobial activity and complexes.

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INTRODUCTION

Mixed ligands complexes is a subject of increasing interest in coordination bioinorganic chemistry. Mixed-ligand complexes containing (2 or more) different ligand molecules generally found to be more active biologically than the free ligand and its binary complexes. (1,2) Many research papers have been published on preparing of metal complexes with mixed ligands and characterization (3–5).

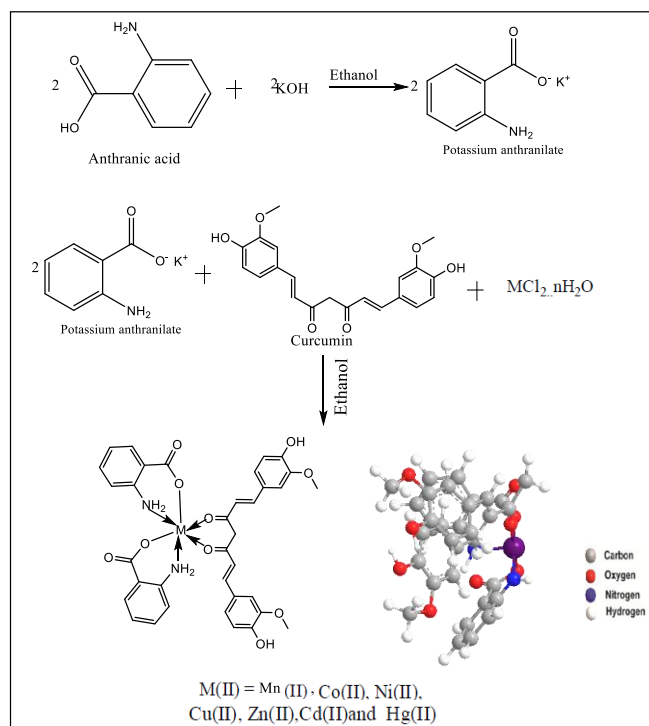
Curcumin, polyphenol a hydrophobic yellow-orange derived from the rhizome of the herb *Curcuma longa*, used in pharmaceutical preparations and food(6,7) and a very interesting pharmacological compound due to its innumerable pharmacological applications, including anti-inflammation, anti-oxidant, anti-human immune deficiency virus, anti-microbial, anti-mutagenic, anti-parasitic, and anti-cancer (8,9) Curcumin is poorly absorbed in the gut, which limits its bioavailability (10) exhibit many beneficial health effects including its anti-carcinogenic. (11).

Anthranilic acid (Anth.H) is one of the best compound used in the laboratory by degrading ancient dye indigo (12). It is a white solid amino acid(AA) in pure form whereas commercially available in yellow form. Its molecule consists of a benzene ring (C₆H₆) with two adjacent functional (-COO⁻) and (NH₂) groups, (12). The mixed ligand complexes of bio metals with tributylphosphine and (Anth.H) have shown activity against *Staphylococcus*, *Klebsiella* SPP. and *Bacillus* (13). Furthermore, the rhodium complexes with (N-phenyl)-Anthranilic acid ligands are used as catalysts (14).

In this paper, we report synthesis and characterization of seven mixed ligand complexes derived from Curcumin (CUM) and Anthranilic acid (Anth H) using bivalent metals chlorides. The physicochemical and antimicrobial Activities study of this complex should therefore be a good candidate to study and characterize. This is the theme of this work.

EXPERIMENTAL

All the chemicals and solvents were purchased of A.R. Grade quality obtained from (Aldrich and BDH) were used without further purification. All complexes were prepared in general procedure (15) are schematically presented in scheme 1.



Scheme 1: The synthesis route of Metal Mixed Ligand Complexes

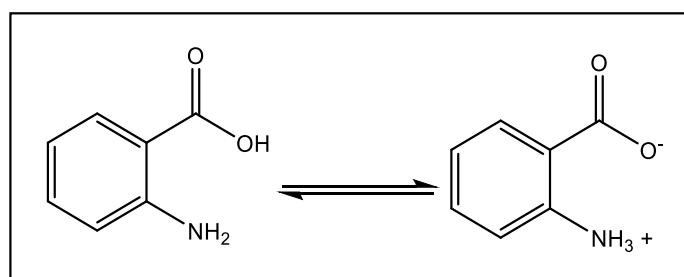
RESULTS AND DISCUSSION

The complexes are air-stable, and the metal analysis (M %) of the complexes is approximate with the calculated results from the empirical formula of each complex and exhibit various shades of color: The solubility of the complexes in the seven solvents (H₂O, acetone, benzene, methanol, ethanol, hexane and DMSO) used, varied according to M (II) used: All complexes were insoluble in benzene, hexane, water, and soluble in all the solvents. The high (M.P/De.)°C are shown in Table 1. The molar conductivity ($\text{ohm}^{-1} \cdot \text{cm}^2 \cdot \text{mol}^{-1}$) of all complexes solutions measurements ($1 \times 10^{-3} \text{M}$ in DMSO as solvents all complexes are non-electrolytes (16)). All of the complexes in this paper are paramagnetic except [Zn(II), Cd(II), & Hg(II)] complexes and their magnetic moments (μ_{eff}) are given in Table 2.

The electronic spectra of all the complexes solutions under study were recorded in (10^{-3}M) in (DMSO) at room temperature summarized in Table (2).

The (U.V-Vis) spectrum for the (CUM) exhibits two absorption peaks at ($\lambda_{\text{max}} 268 \text{ nm}$) (37313 cm^{-1}) is assigned to ($\pi \rightarrow \pi^*$), and ($\lambda_{\text{max}} 434 \text{ nm}$) (23041 cm^{-1}) is assigned to ($n \rightarrow \pi^*$) transitions in the ketone (C=O) group. Thus, the $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ absorptions of (CUM) move close to each other agree with data reported by several research workers, (12–21). A observed a shift in positions of these bands is when these β -keto compounds are engaged in complex formation with metals through β -C=O group. Apart from these bands some specific bands are also observed in case of all complexes which are listed as below in Table 3. The (U.V-Vis) spectrum for the (Anth.H) exhibits (2) absorption peaks at ($\lambda_{\text{max}} 242 \text{ nm}$) (41322 cm^{-1}) & ($\lambda_{\text{max}} 332 \text{ nm}$) (30120 cm^{-1}) which are appointed to ($\pi \rightarrow \pi^*$), and ($n \rightarrow \pi^*$) transition respectively (22).

The chelation of (Anth.H) as evidently present in its (zwitterion form) &, therefore, the N-H moiety must be protonated, generating a (NH_3^+) group whereas the (COO^-) group remains in the anionic form, and the FT-IR spectra of these cannot be compared entirely with those of chelates as L- amino acids in complexes do not exist as zwitterions. Scheme (2)



Scheme (2): Zwitterion of Anthranilic acid

The IR (KBr), spectrum (ν , cm^{-1}) for (AnthH) showed a characteristic carboxylic acid (-COO) absorption, owing to (OH) stretching at 3240 cm^{-1} , Displayed peak at 3321 cm^{-1} , owing to (NH_2) group. In addition, recorded a peak at 1662 cm^{-1} and 1485 cm^{-1} owing to (-COO)_{asym} and (-COO)_{sym} respectively with (-COO)_{asym} - (-COO)_{sym} = 177 . and a peak displayed at 1716 cm^{-1} , assigned for (C=O) acid stretching.

The spectrum (ν , cm^{-1}) for (CUM) recorded strong band at (3444) cm^{-1} which is signed to hydrogen bonded $\nu(\text{OH})$ phenolic and a peak at 2480 cm^{-1} due to asym. ν (C-O-C) stretching, also, an additional peak at 10268 cm^{-1} , owing to sym ν (C-O-C) stretching, a distinct peak for ν (Ar-O-CH₃) recorded at 1254 cm^{-1} . and $1469, \text{ cm}^{-1}$ ν (C=C) str, 841 cm^{-1} out of plain ν (C-H benz.) The peaks of weak intensity observed in the regions [$513\text{-}520$] cm^{-1} and [$459\text{-}470$] cm^{-1} can be owing to $\nu(\text{M-O})$ and $\nu(\text{M-N})$ present in the complexes respectively.

The (Anth) act as uninegative bidentate ligand in which carbonyl oxygen of the acid group and nitrogen of the secondary amine group is coordinated to the metal ion.

However the (CUM) ligand coordinates in bidentate fashion via its two keto (C=O) moieties. Electronic spectra and magnetic moment of the complexes confirmed the octahedral geometry for the

complexes.

Table (1): Some Physical properties of the complexes

Compounds Chemical Formula)	M. wt Calc.	Color	Yield %	M .p °c (de)°c	Am (ohm ⁻¹ .cm ² .mol ⁻¹) in (DMSO 10 ⁻³ M.	Metal% (exp)
[Mn(CUM)(Anth)2]	695.57	Yellow	65	>260	11.4	7.90 (8.8)
[Co(CUM)(Anth)2]	699.57	Brown	60	180	11.1	8.42 (9.7)
[Ni(CUM)(Anth)2]	699.33	Yellow	90	>260	10.6	8.39 (8.9)
[Cu(CUM)(Anth)2]	704.18	Green	75	171	10.8	9.02 (9.8)
[Zn(CUM)(Anth)2]	706.05	Yellow	77	>260	9.5	9.26 (10.5)
[Cd(CUM)(Anth)2]	753.05	Yellow	75	>260	7.9	14.93 (15.6)
[Hg(CUM)(Anth)2]	841.23	Yellow	74	>260 (de)	7.7	23.84 (25.4)

Table (2): Electronic spectral Data of compounds

Comp.	Nm	u' cm-1	ε max mol-1 . L.cm-1	Assignments	μ _{eff} B.M
Anth.	242 332	41322 30120	1857 1924	π → π* n→π*	-
CUM	268 434	37313 23041	599 1589	π → π* n→π*	-
[Mn(CUM)(Anth)2]	263 324 428 451 849	38022 30864 23364 22172 11778	938 1962 227 200 011	L.F C-T 6A1g→4T1g(G) 6A1g→4T2g(G)	5.8
[Co(CUM)(Anth)2]	265 347 428 716	37735 28818 23364 13966	544 1042 27 77	L.f C-T 4T1g → 4T1g (P) (ν3) 4T1g → 4A2g (ν2)	4.5
[Ni(CUM)(Anth)2]	266 428 870	37593 23364 11494	472 420 43	L.f C-T 3A2g(F) → 3T1g(F) (ν3)	3.15
[Cu(CUM)(Anth)2]	271 345 828	36900 28985 12077	1213 479 70	L.f C-T 2Eg→2T2g	1.81
[Zn(CUM)(Anth)2]	262 326 430	38167 30674 23255	869 747 232	Charge transfer Charge transfer n→π	Diamag.
[Cd(CUM)(Anth)2]	262 330	38167 30303	380 1649	Charge transfer Charge transfer	Diamag.

	424	23584	136	$n \rightarrow \pi$	
[Hg(CUM)(Anth) ₂]	268 301 431	37313 33222 23201	888 702 201	Charge transfer Charge transfer $n \rightarrow \pi$	Diamag.

Table (3): Assignment of infrared frequencies in Cm^{-1} of the (Anth.H) kmqi

(N-H) + (O-H)	(NH ₃) ⁺	(C=O)	(C=C)	(COO ⁻) _{asy}	(COO ⁻) _{sy}	Δ -COO ⁻ asy (-COO ⁻ sy)
3321 3240	3110	2962	1496	1662	1485	177

Table (4): Assignment of infrared frequencies in Cm^{-1} of the (CUM)

Phenolic $\nu(\text{OH})$	$\nu(\text{C-H})$ aromatic	$\nu(\text{C-H})$ aliphatic	$\nu(\text{C=O})$	$\nu(\text{C=C})$	(Ar-C=C)	$\nu(\text{C-O-C})$	$\nu(-\text{OCH}_3)$
3444	3066	2935	1597	1454	1438	1157	1133

Table (5): Assignment of infrared frequencies in Cm^{-1} of the [CUM-M-Anth] complexes

Complexese	Phenolic and $\nu(\text{OH})$	$\nu(\text{NH}_2)$	$\nu(\text{C-H})$ aromatic	$\nu(\text{C-H})$ Aliphatic	$\nu(\text{C=O})$ Keton	$\nu(\text{C=O})$ COO ⁻ asy, sym	$\nu(\text{C=C})$	$\Delta \nu$ COO ⁻ (asym-sym)	$\nu(\text{M-N})$	$\nu(\text{M-O})$
[Mn(CUM)(Anth) ₂]	3305	3236 3209	3039	2924	1593	1616 1408	1454	200	515	470
[Co(CUM)(Anth) ₂]	3414	3305 3136	3039	2962	1593	1612 1408	1458	204	516	459
[Ni(CUM)(Anth) ₂]	3305	3128	3008	2924	1593	1612 1408	1458	204	520	470
[Cu(CUM)(Anth) ₂]	3441	4375 3120	3008	2920	1554	1604 1377	1458	227	516	482
[Zn(CUM)(Anth) ₂]	3298	3298 3128	3008	2920	1593	1616 1404	1458	212	516	470
[Cd(CUM)(Anth) ₂]	3483	3290 3240	3078	2920	1589	1616 1400	1450	216	516	466
[Hg(CUM)(Anth) ₂]	3437	3293 3244	3074	2920	1512	1577 1369	1454	208	513	470

Antibiological and antifungal Evaluation

It's evident from the data displayed in tables 5. antibacterial activity against (*Esherichia Coli* and *Bacillus subtilis*) and *andida albicans* antifungal activity. DMSO, which is used as solvent and negative control produced no observable (IZ) t against any of the test pathogen tested. (21) The antibacterial activity is found to be in the order; Results of antibacterial action and fungi of the all compounds are described in photographs of growth inhibition zones are illustrated in figure (1) and explained as follows:

Antibiological

Esherichia Coli : Mn > Cd > Cu > Hg = CUR = Anth.H = Zn= Co= Control

Bacillus Subitils : Hg > Zn Cd > Cu > CUR = Anth.H = Zn= Co= Control

Antifungal activity

Candida albicans is found to be in the order;

Mn > Cd > Cu > Hg > CUR = Anth.H = Zn= Co= Ni= Control

The presence of increases the delocalization of π - electrons over the whole chelate ring. electron (C=O) and N-donor group in the complexes also plays a role in enhancing the inhibition activity. (21,23)

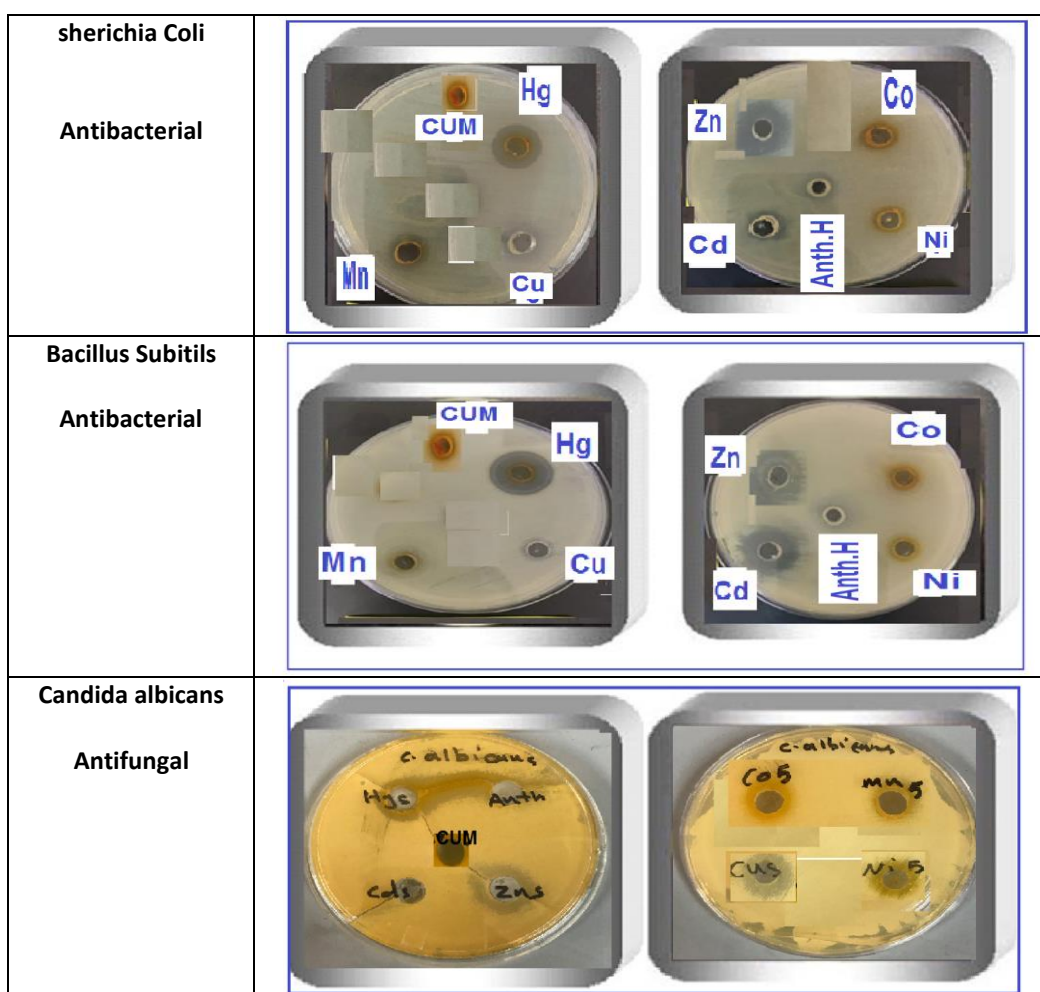
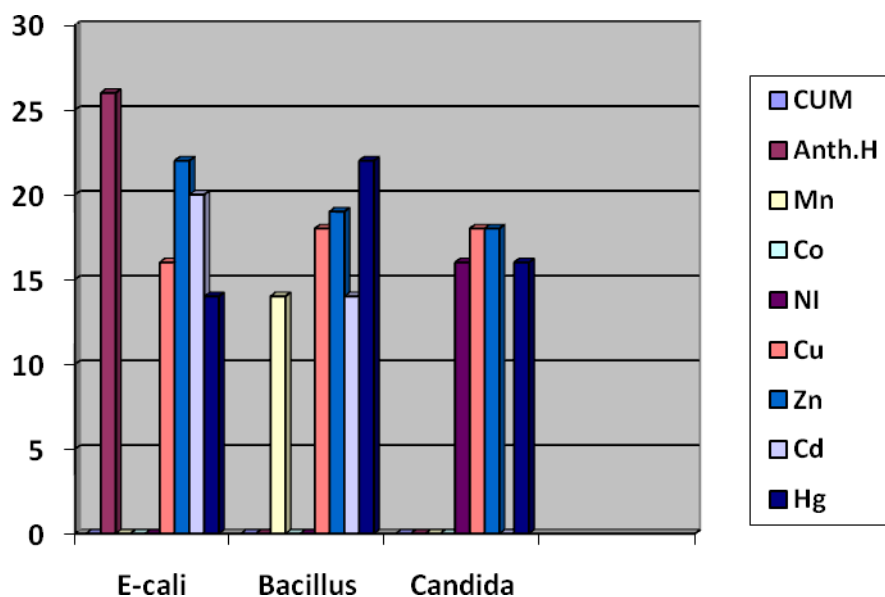


Figure (1): Antibacterial and antifungal activities of studied compounds



Scheme (3): Chart of biological effects of the studied compounds

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