

Original Research Article

Synthesis and Biological Study of Substituted 2''-Hydroxy, 2'',4''-dichloro Chalcones and Their Co(II), Cu(II) and Ni(II) Complexes for Their Antioxidant and Antimicrobial Potentials

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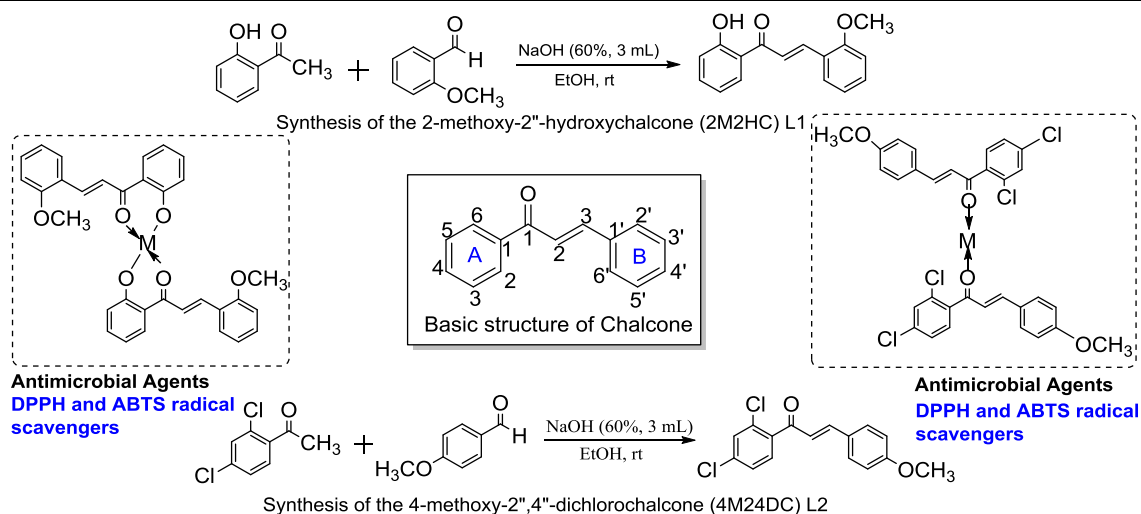
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ABSTRACT

2-methoxy-2''-hydroxychalcone (2M2HC) and 4-methoxy-2'',4''-dichlorochalcone (4M24DC) and their metal complexes were synthesized, characterized, and confirmed by melting point, FT-IR, UV-Visible, ¹H-NMR, EIMS, and AAS spectroscopic techniques. The elemental analysis was done and found following the calculated values. Metal(II) complexes, [M(L₁₋₂)₂], [where M = Ni(II), Cu(II), Co(II); L = 2-methoxy-2''-hydroxychalcone (2M2HC) and 4-methoxy-2'',4''-dichlorochalcone (4M24DC)] were subsequently prepared. The biological evaluation of the synthesized chalcone derivatives and their metal complexes was done. They were screened for antioxidant and antimicrobial activities. Overall, the ligands (chalcones) and metal complexes demonstrated good to moderate antioxidant and antimicrobial activities.

GRAPHICAL ABSTRACT



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Introduction

Chalcones (1,3-diphenyl-2-propen-1-ones) are precursors for synthesizing many organic compounds (heterocyclic compounds) with yellow as the primary characteristic color.

They occur as either *trans* (*E*) or *cis* (*Z*) isomers having two aromatic rings that are connected by a three-carbon α,β -unsaturated carbonyl system [1]. The *E* isomer is more stable thermodynamically, making it the predominant configuration among the chalcones (Figure 1).

The α,β -unsaturated carbonyl group and the substituents attached to each aromatic ring are responsible for the numerous biological properties of the chalcones, including antioxidant, anti-inflammatory, cytotoxic,

anticancer, analgesic, antihyperglycemic, antimicrobial, antimalarial, and antileishmanial activities. The chalcones have been synthesized via the Claisen-Schmidt condensation reaction [2]. The method is routinely carried out in an alkaline alcoholic solution at room temperature.

Other methods are Suzuki coupling reaction, Carbonylative heck reaction, Ultrasound irradiation, Microwave irradiation, Solvent-free reaction, Friedel-Crafts acylation, and Wittig reaction [3]. The Claisen-Schmidt method was adopted in this study because it's simple, a product obtained is of high purity, has a high yield, and has little or no side or by-product [4]. The basic structure of the chalcone is presented in Figure 1.

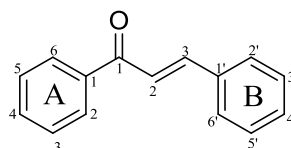


Figure 1. The basic structure of chalcone

Syam *et al.* reported some chalcones' preparation, characterization, and in vitro cytotoxicity against various human cell lines. Most of the compounds prepared were active cytotoxic agents [5]. Sumathi *et al.* synthesized some metal complexes of 2-hydroxyphenyl-3-(1H-indol-3-yl)-prop-2-en-1-one). Elemental analysis, magnetic susceptibility, molar conductance, I.R., UV-Vis, NMR, Mass, and ESR spectroscopic studies on the ligand (chalcone) and their metal complexes were carried out. Antimicrobial activities indicated that only a few complexes exhibit significant activity. The nuclease activity studies showed that the complexes bind to the DNA [6]. Hussien *et al.* reported new derivatives of Cu(II), Co(II), and Ni(II) complexes with 2''-hydroxychalcones as ligands. Antimicrobial screening of the synthesized compounds showed enhanced metal complexes' activity compared to their corresponding ligands [7]. Tabti *et al.* reported the successful synthesis and characterization of

new derivatives of metallic complexes of a chalcone. The synthesis of the chalcone was done by the condensation of dehydroacetic acid (DHA) with Indol-3-carboxaldehyde. The synthesized compounds were characterized by FT-IR, UV-Vis, ESR, single crystal XRD, and Mass spectrometry [8]. Kocyigit *et al.* synthesized and characterized a series of chalcone-imide derivatives. Biological evaluation of the synthesized compounds as anticancer agents, antimicrobial agents, carbonic anhydrase, and acetylcholinesterase enzyme inhibitors was investigated [9].

Research Methodology

Materials

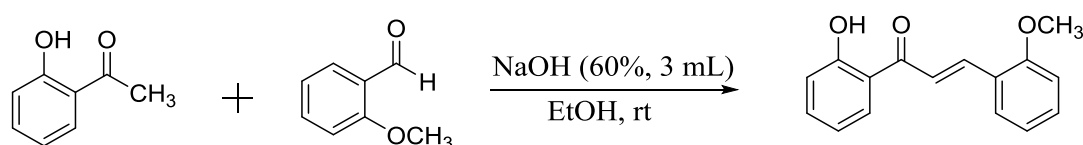
Ultra-high purity Sigma-Aldrich chemicals were purchased and used as received. The mass spectra were obtained from MAT 312 and MAT 113D mass spectrometer. The ^1H -NMR spectra were recorded on Bruker AM machines operating at 400 MHz. The infra-red spectra were obtained

from PerkinElmer Spectrum Version 10.4.3. The UV-Visible spectra were recorded on a Shimadzu UV-2600 series (230 V) spectrophotometer. The percentage compositions of the metals in the metal complexes were obtained from a Shimadzu AA-6200 Spectrophotometer.

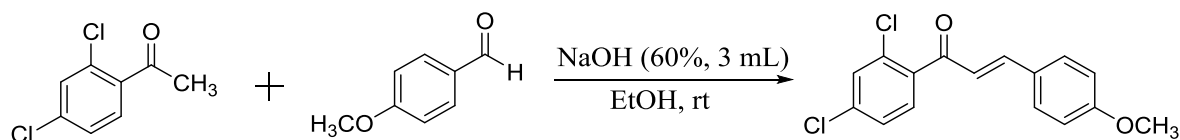
Synthesis of chalcones

The method reported by Bale *et al.* was adopted to prepare the compounds [10]. To a stirred solution of substituted acetophenone (1 mmol) in ethanol (10 mL), a solution of sodium hydroxide

(60%, 3 mL) was added drop-wise. The reaction mixture was initially stirred for 30 min at room temperature. Substituted benzaldehyde derivative (1 mmol) was added to the mixture and stirred at room temperature until crystals or precipitates appeared. The reaction was monitored by thin-layer chromatography (TLC). Upon completion of the reaction, ice-cold water was added to the reaction mixture. The resulting solids were filtered and washed with an excess of distilled water and air-dried to afford an analytical sample.



Scheme 1. Synthesis of the 2-methoxy-2''-hydroxychalcone (2M2HC) **L₁**



Scheme 2. Synthesis of the 4-methoxy-2''-4''-dichlorochalcone (4M24DC) **L₂**

Synthesis of metal complexes

The method reported by Tabti *et al.* was adopted to prepare the metal complexes.

Metal(II) chloride (0.25 mmol, 5 mL, CH₃OH) was added to the solution of the ligand (0.5 mmol, 10 mL, CHCl₃). The reaction mixture was refluxed for 2 h. Methanolic ammonia solution

was added to the reaction mixture. The reaction mixture was refluxed for 4 h for proper completion formation. The solution obtained after the reaction time was cooled at room temperature. The solid separated was filtered and washed successively with ethanol and diethyl ether to afford an analytical sample.

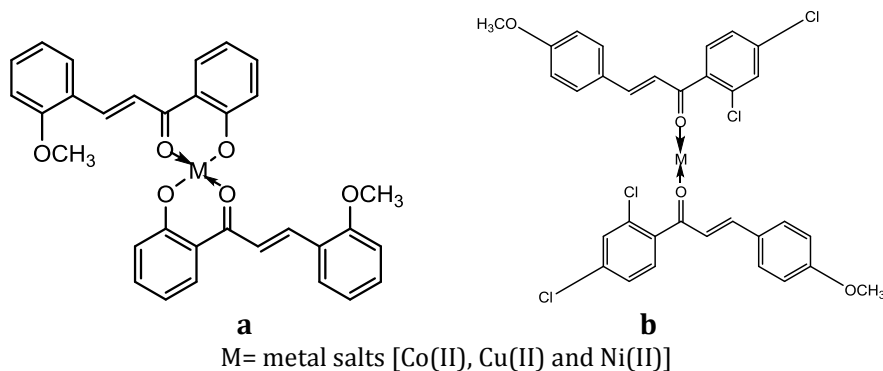


Figure 2. (a) Probable structure of the complexes of **L₁** (b) Probable structure of the complexes of **L₂**

Biological evaluation

Antioxidant activity

In vitro evaluation of the antioxidant activities of the 2-methoxy-2''-hydroxychalcone (2M2HC), 4-methoxy-2'',4''-dichlorochalcone (4M24DC) and their complexes. The antioxidant potentials of the chalcones and their metal complexes were determined using DPPH (2,2-diphenyl-1-picrylhydrazyl) and ABTS (2,2''-azino-bis(3-alkylbenzothiazoline-6-sulphonic acid) radicals [11].

Antimicrobial activity

In vitro antimicrobial activity studies of the 2-methoxy-2''-hydroxychalcone (2M2HC), 4-methoxy-2'',4''-dichlorochalcone (4M24DC) and their metal complexes. The *in vitro* antimicrobial activities of the chalcones and their complexes against *Staphylococcus aureus*, *Bacillus subtilis*, *Pseudomonas aeruginosa*, *Candida albicans*, *Aspergillus niger*, and *Penicillium citrinum* were determined using the agar well diffusion method [6].

Results

Spectroscopic data of chalcones (2M2HC and 4M24DC)

2M2HC [(E)-1-(2-hydroxyphenyl)-3-(2-methoxyphenyl)prop-2-en-1-one]:

Yellow solid; Yield: 2.0 g, 78.65%; M.p.: 109-111 °C; ¹HNMR (400 MHz, Chloroform-*d*) δ 12.94 (s, 1H, -OH), 8.23 (d, *J* = 15.6 Hz, 1H, β-olefinic proton), 7.79 (d, *J* = 15.6 Hz, 1H, α-olefinic proton), 6.88–7.93 (m, 8H, Ar-H), 3.95 (s, 3H, -OCH₃); ¹³C NMR (101 MHz, Chloroform-*d*) δ 194.46, 163.72, 159.19, 141.29, 136.29, 132.35, 129.85, 129.80, 123.78, 120.95, 120.93, 120.35, 118.89, 118.70, 111.46, 55.75; EI-MS: *m/z* (rel. abund.%), 253 (M⁺, 100), 254 (25); Elemental analysis (micro-analytical data); Theoretically calculated for C₁₆H₁₄O₃: C, 75.58; H, 5.55; O, 18.88; Found: C, 75.56; H, 5.53; O, 18.86. FT-IR: 3316 (-OH), 3088 (C-H, Aromatic), 1664 (C=O), 1575 (C=C), 1171 (-OCH₃), 1464 (CH=CH, Vinyl) 4M24DC [(E)-1-(2,4-dichlorophenyl)-3-(4-methoxyphenyl)prop-2-en-1-one]:

Pale yellow solid; Yield: 3.03 g, 98.64%; M.p.: 94-96 °C; ¹HNMR (400 MHz, Chloroform-*d*) δ 7.48 (d, *J* = 1.9 Hz, 1H, β-olefinic proton), 7.35 (d, *J* = 1.9 Hz, 1H, α-olefinic proton), 6.91–7.53 (m, 7H, Ar-H), 3.85 (s, 3H, -OCH₃); ¹³C-NMR (101 MHz, Chloroform-*d*) δ 192.78, 162.22, 146.74, 137.84, 136.73, 132.38, 130.60, 130.40, 130.23, 127.32, 127.05, 123.83, 114.63, 55.55; EI-MS: *m/z* (rel. abund.%), 307 (M⁺, 55), 309 (M+2, 35), 311 (M+4, 10); Elemental analysis (micro-analytical data); Theoretically calculated for C₁₆H₁₂Cl₂O₂: C, 62.56; H, 3.94; O, 10.42; Found: C, 62.54; H, 3.89; O, 10.38. FT-IR: 3071 (C-H, Aromatic), 1655 (C=O), 1589 (C=C), 1178 (-OCH₃), 824 (Ar-Cl), 1465 (CH=CH, Vinyl)

Table 1. Analytical and physical data of chalcone (2M2HC) and its complexes

Compounds	Molecular formula	Molecular weight	Colour	Yield %	M.P. (°C)	Elemental analysis (CHMO)			
						Found (Calcd)			
						C	H	O	M
2M2HC	C ₁₆ H ₁₄ O ₃	254.29	Yellow	78.65	109-111	75.56 (75.58)	5.53 (5.55)	18.86 (18.88)	—
2M2HCNi	C ₃₂ H ₃₀ NiO ₈	601.28	Greenish yellow	70.76	224-226	63.36 (63.41)	4.97 (4.99)	21.11 (21.12)	10.22 (10.48)
2M2HCCu	C ₃₂ H ₃₀ CuO ₈	606.13	Light green	72.41	239-241	63.88 (63.92)	4.99 (5.03)	21.28 (21.29)	9.54 (9.76)
2M2HCCo	C ₃₂ H ₂₆ CoO ₆	565.49	Bluish yellow	70.73	214-216	67.94 (67.97)	4.59 (4.63)	16.96 (16.98)	10.12 (10.42)

Table 2. Spectroscopic data of chalcone (2M2HC) and its metal complexes

Ligand and Metal Complexes	$\nu(\text{OH})$ cm^{-1}	$\nu(\text{OH})$ (H_2O) cm^{-1}	$\nu(\text{C}=\text{O})$ cm^{-1}	$\nu(\text{C}=\text{C})$ cm^{-1}	$\nu(\text{C}-\text{O})$ cm^{-1}	$\nu(\text{M}-\text{O})$ cm^{-1}	UV-Vis (λ_{max}) Solvent: Methanol	
							$\pi-\pi^*$	$n-\pi^*$
2M2HC	3316	-----	1664	1575	1252	-----	289	366
[Ni(2M2HC) ₂].2H ₂ O	-----	3212	1637	1579	1249	428	253, 285	306, 363
[Cu(2M2HC) ₂].2H ₂ O	-----	3322	1627	1576	1243	470	284	343
[Co(2M2HC) ₂]	-----	-----	1689	1573	1250	463	252, 287	362

Table 3. Analytical and physical data of chalcone (4M24DC) and its metal complexes

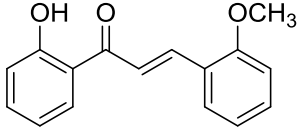
Compound	Molecular formula	Molecular weight	Colour	%Yield	M.P. ($^{\circ}\text{C}$)	Elemental analysis (CHMO) Found (Calcd)			
						C	H	O	M
4M24DC	$\text{C}_{16}\text{H}_{12}\text{Cl}_2\text{O}_2$	307.17	Pale Yellow	98.64	94-96	62.54 (62.56)	3.89 (3.94)	10.38 (10.42)	—
4M24DC Ni	$\text{C}_{32}\text{H}_{28}\text{Cl}_4\text{NiO}_6$	709.06	Light green	85.76	237-239	53.78 (53.84)	3.86 (3.95)	12.98 (13.45)	8.72 (8.90)
4M24DC Cu	$\text{C}_{32}\text{H}_{28}\text{Cl}_4\text{CuO}_6$	713.92	Blue	83.79	226-228	53.89 (54.20)	3.96 (3.98)	13.51 (13.54)	8.02 (8.28)
4M24DC Co	$\text{C}_{32}\text{H}_{28}\text{Cl}_4\text{CoO}_6$	709.30	Light blue	75.45	205-207	54.13 (54.19)	3.87 (3.98)	13.48 (13.53)	8.12 (8.31)

Table 4. Spectroscopic data of chalcone (4M24DC) and its metal complexes

Ligand and Metal Complexes	$\nu(\text{OH})$ (H_2O) cm^{-1}	$\nu(\text{C}=\text{O})$ cm^{-1}	$\nu(\text{C}=\text{C})$ cm^{-1}	$\nu(\text{C}-\text{O})$ cm^{-1}	$\nu(\text{M}-\text{O})$ cm^{-1}	UV-Vis (λ_{max}) Solvent: Methanol	
						$\pi-\pi^*$	$n-\pi^*$
4M24DC	----	1655	1589	1257	----	242	344
[Ni(4M24DC) ₂].2H ₂ O	3219	1633	1571	1250	515	246	342
[Cu(4M24DC) ₂].2H ₂ O	3344	1625	1594	1242	425	224	363
[Co(4M24DC) ₂].2H ₂ O	3548	1653	1585	1248	415	246, 282	372

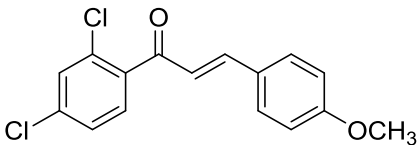
Antioxidant activity: Results of *in vitro* antioxidant (DPPH and ABTS) assay of the chalcones (2M2HC and 4M24DC) and their metal complexes are presented as follows;

Table 5. DPPH and ABTS radical scavenging activity of 2M2HC and its complexes

S/N	Compound	Structure	IC ₅₀ (μM) DPPH	ABTS
1	2M2HC		24.23 \pm 0.0166	19.08 \pm 0.0059
2	2M2HCCo		14.71 \pm 0.0059	14.78 \pm 0.0080
3	2M2HCCu		16.26 \pm 0.0195	18.16 \pm 0.0145
4	2M2HCNi		11.02 \pm 0.0022	25.31 \pm 0.0050
			Ascorbic acid	Ascorbic acid
			5.52\pm0.0026	3.53\pm0.0059

*Values are indicated as mean \pm SEM (n=3)

Table 6. DPPH and ABTS radical scavenging activity of 4M24DC and its complexes

S/N	Compound	Structure	IC ₅₀ (μM) DPPH	ABTS
1	4M24DC		19.04±0.0054	31.83±0.0205
2	4M24DCCo		9.00±0.0214	22.56±0.0087
3	4M24DCCu		2.49±0.0040	13.28±0.0076
4	4M24DCNi		14.92±0.0181	20.37±0.0040
			Ascorbic acid	Ascorbic acid
			5.52±0.0026	3.53±0.0059

*Values are indicated as mean±SEM (n=3)

Antimicrobial Activity: Results of *in vitro* (2M2HC and 4M24DC) and their complexes are antimicrobial activity studies of the chalcones presented as follows;

Table 7. Average zone of inhibition of 2M2HC and its complexes

Compound Code	Candida albicans (mm)	Aspergillus niger (mm)	Penicillium citrinum (mm)
2M2HC	11.00	11.00	12.00
2M2HCCo	10.50	6.00	12.00
2M2HCNi	12.00	8.50	10.50
2M2HCCu	11.00	9.50	12.00
DMSO (negative control)	-	-	-
Fluconazole (positive control)	35.00	17.00	14.00

*Compound: ≥ 14 mm, significant; 10-13 mm, moderate; <10mm, weak; “—” represent “inactive”

Table 8. Average zone of inhibition of 4M24DC and its complexes

Compound Code	Candida albicans (mm)	Aspergillus niger (mm)	Penicillium citrinum (mm)
4M24DC	10.00	11.00	-
4M24DCNi	11.00	11.50	-
4M24DCCu	14.50	8.50	-
4M24DCCo	12.00	10.50	-
DMSO (negative control)	-	-	-
Fluconazole (positive control)	35.00	17.00	14.00

*Compound: ≥ 14 mm, significant; 10-13 mm, moderate; <10mm, weak; “—” represent “inactive”

Table 9. Average zone of inhibition of 4M24DC and its complexes

Compound Code	Staphylococcus aureus (mm)	Bacillus subtilis (mm)	Pseudomonas aeruginosa (mm)
4M24DC	-	2.00	7.50
4M24DCNi	13.00	6.00	-
4M24DCCu	15.50	5.00	6.50
4M24DCCo	12.00	3.00	-
DMSO (negative control)	-	-	-
Streptomycin (positive control)	30.00	25.00	23.00

*Compound: ≥ 14 mm, significant; 10-13 mm, moderate; <10mm, weak; “—” represent “inactive”

Table 10. Average zone of inhibition of 2M2HC and its complexes

Compound Code	<i>Staphylococcus aureus</i> (mm)	<i>Bacillus subtilis</i> (mm)	<i>Pseudomonas aeruginosa</i> (mm)
2M2HC	-	4.00	-
2M2HCCo	-	-	-
2M2HCCu	-	-	-
2M2HCNi	-	-	-
DMSO (negative control)	-	-	-
Streptomycin (positive control)	30.00	25.00	23.00

*Compound: ≥ 14 mm, significant; 10-13 mm, moderate; <10 mm, weak; “—” represent “inactive”

Discussion

Chalcone Derivatives

Scheme 1 and 2 represent the synthesis of the two chalcone derivatives (2M2HC and 4M24DC). Substituted acetophenones were reacted with substituted benzaldehydes to afford the chalcone compounds. The reactions were carried out at room temperature in an alkaline medium (60% NaOH). The extent of the reaction was monitored using TLC. The chalcones were characterized by FT-IR, $^1\text{H-NMR}$, and EI-MS spectroscopic techniques. Elemental (CHN) analysis was done as well.

The compounds' infrared absorption spectra were recorded on a PerkinElmer Spectrum Version 10.4.3 and Bruker spectrometer. The chalcone derivatives' characteristic carbonyl group (C=O) appeared between $1654\text{--}1663\text{ cm}^{-1}$ in the functional group region [12-13, 5, 7]. The carbon-carbon double bond (C=C) appeared as a prominent band mostly between $1575\text{--}1589\text{ cm}^{-1}$ wavenumber (cm^{-1}) [5, 7]. The region at which other absorption bands appear depends on the type and position of the substituents present on the aromatic rings [12-13].

The $^1\text{H-NMR}$ spectra of the chalcone compounds were recorded in deuterated DMSO- d_6 and CDCl_3 on a 400 MHz machine. The H- α and H- β protons of the chalcones occur as two doublets in the ranges $7.35\text{--}7.79\text{ ppm}$ (H- α) and $7.48\text{--}8.23\text{ ppm}$ (H- β) in the $^1\text{H-NMR}$ spectra [14, 5]. The aromatic protons appeared in the range of δ

$6.88\text{--}7.93$, depending on the type and position of the substituents present on the aromatic rings.

The mass spectra of the compounds (2M2HC and 4M24DC) displayed the molecular ion peak $[\text{M}]^+$ at m/z 253 and 307, representing the actual molecular weights of the molecules. The micro-analytical (CHN) data obtained was following the calculated values.

Chalcone metal complexes

Metal(II) complexes $[\text{M}(\text{L}_{1-2})_2]$, [where $\text{M}=\text{Ni(II)}$, Cu(II) , Co(II) ; $\text{L}_1=2\text{-methoxy-2''-hydroxychalcone}$ (2M2HC) and $\text{L}_2=4\text{-methoxy-2'',4''-dichlorochalcone}$ (4M24DC)] were synthesized and characterized by melting point, infra-red spectroscopy, UV-Vis spectroscopy, atomic absorption spectroscopy (%M) and elemental (CHO) analyses. Figure 2 represents the probable structures of the metal complexes of the chalcones.

Infra-red spectral analysis of 2M2HC (ligand) and its complexes

The presence of the carbonyl (C=O) in the ligand (2M2HC) is confirmed by an absorption band at 1664 cm^{-1} . This band is shifted to lower or higher wavenumber ($1627\text{--}1689\text{ cm}^{-1}$) in the metal complexes, indicating the carbonyl oxygen's coordination to the metal [7, 15, 13]. New intense broad bands (3212 and 3322 cm^{-1}) appeared in the infra-red spectra of the metal complexes (nickel and copper, respectively) due to the

presence of coordinated water molecules [16-17]. This is absent in the infra-red spectrum of the Cobalt metal complex. An intense absorption band appeared at 1252 cm^{-1} assigned to $\nu(\text{C-O})$ in the ligand is shifted to lower wavenumber ($1243\text{-}1250\text{ cm}^{-1}$) in the infra-red spectra of the metal complexes. Another new absorption band appeared in the infra-red spectra of the metal complexes (Ni, Cu, and Co) in the range of ($428\text{-}470\text{ cm}^{-1}$) assigned to $\nu(\text{M-O})$. This is absent in the infra-red spectrum of the ligand [18] (Table 2).

UV-Visible Spectroscopic Analysis of 2M2HC (ligand) and its Complexes

The UV-Visible absorption band observed for the ligand (2M2HC) at 289 nm was assigned to $\pi\text{-}\pi^*$ aromatic group transitions (conjugated double bonds) [8]. The electronic transition at 366 nm was assigned to $n\text{-}\pi^*$ carbonyl group transition. The $\pi\text{-}\pi^*$ electronic transitions observed for the cobalt, copper, and nickel complexes were found at a lower wavelength in the range 252–287 nm. The $n\text{-}\pi^*$ electronic transitions for the metal complexes were also observed at a lower 343–363 nm wavelength. These displacements occurred due to the coordination of the carbonyl group with the metal. Overall, The UV-Visible absorption spectra indicate the absorption bands characteristic of the ligand as well as the appearance or modification of some new bands characteristic of the metal complexes [8] (Table 2).

Infra-red spectral analysis of 4M24DC (ligand) and its complexes

The presence of the carbonyl (C=O) in the ligand (4M24DC) is confirmed by an absorption band at 1655 cm^{-1} . This band is shifted to the lower wavenumber ($1625\text{-}1653\text{ cm}^{-1}$) in the metal complexes, indicating the carbonyl oxygen's coordination to the metal [7, 15, 13]. New intense

broad bands ($3219\text{-}3548\text{ cm}^{-1}$) appeared in the infra-red spectra of the metal complexes due to the presence of coordinated water molecules [16-17]. An intense absorption band appeared at 1257 cm^{-1} assigned to $\nu(\text{C-O})$ in the ligand is shifted to lower wavenumber ($1242\text{-}1250\text{ cm}^{-1}$) in the infra-red spectra of the metal complexes. Another new absorption band appeared in the infra-red spectra of the metal complexes (Ni, Cu, and Co) in the range of ($415\text{-}515\text{ cm}^{-1}$) assigned to $\nu(\text{M-O})$. This is absent in the infra-red spectrum of the ligand [18] (Table 3).

UV-Visible Spectroscopic Analysis of 4M24DC (Ligand) and its Metal Complexes

The UV-Visible absorption band observed for the ligand (4M24DC) at 242 nm was assigned to $\pi\text{-}\pi^*$ aromatic group transitions (conjugated double bonds) [8]. The electronic transition at 344 nm was assigned to $n\text{-}\pi^*$ carbonyl group transition. The $\pi\text{-}\pi^*$ electronic transitions observed for the cobalt, copper, and nickel complexes were found at a lower wavelength (224 nm) for the copper complex but a higher wavelength for cobalt (246 nm) and nickel (282 nm) complexes. The $n\text{-}\pi^*$ electronic transitions for the metal complexes were observed at a lower wavelength (342 nm) for the cobalt complex but at a higher wavelength for the copper (363 nm) and nickel (372 nm) complexes. These displacements are due to the carbonyl group's coordination with metal ions. Overall, The UV-Visible absorption spectra indicate the absorption bands characteristic of the ligand and the appearance or modification of some new bands characteristic of the metal complexes [8] (Table 3).

Antioxidant Activity Studies

The ligands (2M2HC and 4M24DC) and complexes were screened for their antioxidant potentials. They were subjected to 2,2-diphenyl-1-picrylhydrazyl (**DPPH**) and 2,2'-azino-bis(3-

alkylbenzothiazoline-6-sulphonic acid (ABTS) assays (Table 5 and 6). The antioxidant potentials of the chalcones and their metal complexes were evaluated to determine their relative abilities to scavenge the two free radicals (DPPH and ABTS). It is worth mentioning that the antioxidant (DPPH and ABTS) activity of the chalcone compound was enhanced after binding to a metal.

The copper complex of (*E*)-1-(2,4-dichlorophenyl)-3-(4-methoxyphenyl)prop-2-en-1-one (4M24DCCu) was identified as the best antioxidant (DPPH radical scavenger) amongst the metal complexes investigated. The complex exhibited higher DPPH radical scavenging activity ($IC_{50}=2.49\pm0.0040$) than the standard ascorbic acid ($IC_{50}=5.52\pm0.0026\ \mu\text{M}$).

In all cases, the metal complexes exhibited better activities than the ligands (chalcones). The enhanced activity may be due to the presence of electron-rich metals and electron-releasing groups like the $-\text{OCH}_3$ and $-\text{OH}$ groups.

Antimicrobial Activity Studies

The average zones of inhibition (in mm) of the compounds (2-methoxy-2''-hydroxychalcone, 4-methoxy-2'',4''-dichlorochalcone and their metal complexes) against *S. aureus*, *B. subtilis*, *P. aeruginosa*, *C. albicans*, *A. niger*, and *P. citrinum* are presented in Tables (7-10).

The observed zones of inhibition (in mm) indicated that the metal complexes demonstrated better activities than the chalcones in almost all cases. The chelation theory and size of the metal ion supported the increase in activity [19-20]. The improved activity of the metal complexes can also be further explained based on the overtone theory [21]. According to the overtone theory of cell permeability, the lipid membrane surrounding the cell favours the passage of only lipid-soluble materials, which is an essential factor determining the extent of antimicrobial activity.

Conclusion

2-methoxy-2''-hydroxychalcone (2M2HC), 4-methoxy-2'',4''-dichlorochalcone (4M24DC), and their metal complexes were synthesized and characterized by physical, analytical, and spectroscopic techniques. The antimicrobial and antioxidant activities of the chalcones and their complexes supported their potential as biologically active molecules. The confirmed bioactive compounds from this study can be utilized as viable templates in drug design and discovery.

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No potential conflict of interest was reported by the authors.

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