



Preparation of New Complexes from a Mixture of Aspirin (acetylsalicylic acid), Paracetamol and Methyldopa with Divalent Manganese, Iron, Cobalt, Nickel and Copper, With a Study of Their Physical and Chemical Properties



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Abstract:

New complexes with a mixture of aspirin (acetylsalicylic acid) with methyldopa or paracetamol with methyldopa were synthesized via the reflux of reaction mixture using a basic medium to deprotonate the ligands. These new complexes of Mn(II), Fe(II), Co(II), Ni(II) and Cu(II) with a mixture of aspirin (acetylsalicylic acid), paracetamol and methyldopa have characterized using FTIR, UV-visible spectra, magnetic susceptibility, flame atomic absorption, C.H.N.S analysis and melting points measurements. The two mixed ligands have been found to act as bidentate chelating agents. Aspirin (acetylsalicylic acid) complexes coordinate to the metal ions through the oxygen of Aspirin's ester group and oxygen of the carboxyl group, while Methyldopa as ligand is coordinated through the oxygen of the carboxyl group and the nitrogen of the amide groups. The Paracetamol was coordinated through the oxygen atom of carboxyl group and the nitrogen atom of the amide group. The stability of these new complexes depends on the size of the chelate rings, thus these ligands with a flexible organic backbone and their complexes contain five and six membered chelate rings, which have almost no strain. The molar conductance measurements for the metal complexes show non-electrolytic behavior in DMF solvent. The all-synthesized complexes which show non-electrolytic properties, also were no conducting electrical current behaved as bi-dentate with octahedral geometrical isomers.

Keywords: Aspirin (acetylsalicylic acid), Paracetamol, Methyldopa, IR, UV, Spectrum of flame.

1. Introduction:

Synthetic study of complexes derived from transition metal and mixed ligands have been of increasing interest especially as antimicrobial activity^[1,2]. Mixed pharmaceutical active molecules play an important role as ligands in complexation with numerous transition state. Numerous transition metals with mixed drugs molecules complexes show wide-ranging pharmaceutical activity, which place them in several biochemical processes^[3] and anti-various agents^[4]. Many methods were published for preparing of the mixed ligands metal complexes. NMR spectroscopy has been used to elucidate the molecular basis of the action of caffeine (CAF) on the complexation with DNA of mutagens such as ethidium bromide, propidium iodide, proflavine and acridine orange, and anticancer drugs such as actinomycin D and daunomycin^[5]. El-Sherif synthesized copper(II) complexes and the ternary complexes Cu(HMI)L (HMI = 4-Hydroxymethylimidazole, L = amino acid, amides or DNA constituents)^[6]. A series of novel Zn(II) mixed ligands complexes were synthesized and

characterized^[7]. Recently, Okasha and coworkers designed and prepared a novel oligomeric mixed ligand complexes and studied their biological applications and the first example of their nanosized scale^[8]. These mixed complexes models provide information about how biological activity achieve, as well as improve^[9]. One of the most important non-steroidal anti-inflammatory drug (NSAID) is aspirin (acetylsalicylic acid) which is named by IUPAC as 2-acetoxybenzoic acid of analgesic and antifever activity^[10,11]. Also, paracetamol (acetaminophen) is used to for relief pain and fever alone or mixed other medications^[12]. Dose is typically given orally, rectally or intravenously^[13]. Finally, methyldopa also known as aldomet which is used as anti-hypertension^[14]. It is given orally or intravenously. The chemical structures of these three drugs help to act as ligand in coordination with many transition metals as it alone or as a mixture of two of them. Paracetamol (Para), is N-(4-hydroxyphenyl) acetamide as IUPAC name role, which is composed also of two functional groups available as bidentate ligand, the hydroxyl amine oxygen atom and the azomethane nitrogen

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atom at the molecule of ketoxime results from the tautomerization of paracetamol^[15]. Finally, methyldopa (Meth) chemical structure is composed of two functional groups available as bidentate ligands, the oxygen of hydroxyl group and nitrogen of amine group^[15]. Synthesis of complexes derived from two or more ligands that are known as pharmaceutically active medications is a very good strategy to improve both the pharmacokinetic and pharmacodynamics properties of the parent drug^[16]. These mixed ligands and their metal complexes represent useful rules that can be design to overcome the specific restrictions of a broad spectrum of drugs^[16]. The most advantages of those complexes derived from the mixed drugs with transition metals are the increasing solubility and bioavailability as well as reduced side effects and toxicity. Also, by using an active metal complex of two active organic molecule (as ligands) gives dual-action drugs which may be more effective than the parent organic drug and be able to overcome the resistance mechanisms^[17]. Mixed ligand transition metal carbodithioate complexes were shown perfect antibiotic activity against tested pathogenic strains, and when also study for their human toxicity, a moderate cell viability of the RD cells was exhibited against the metal complexes^[18]. The central metal ions in complexes of pharmaceutical active ligands (or even mixed ligands) increase the biological activity of the ligand and the efficacy of the drug molecule therapeutic agents^[19]. The requirements for the discovery of new complexes derived from pharmaceutically active ligands (or mixed ligands) having activity more than the parent ligands itself are increased^[20]. The aim of this work is to synthesis and characterization of novel complexes derived from transition metals: Mn(II), Fe(II), Co(II), Ni(II) or Cu(II) and mixed pharmaceutical active molecules,

aspirin (acetylsalicylic acid), paracetamol or methyldopa, and study of their physical and chemical properties.

2-Experimental:

2.1 Materials and measurement:

All Chemical reagents used were purchased from BDH and used as provided.

All metal(II) salts were used as chlorides, supplied by either Merck or Fluka, also ethanol, dimethylformamide (DMF), diethylether. The FTIR spectra in the range (200–4000) cm^{-1} were recorded as cesium iodide disc on FTIR 8300 Shimadzu Spectrophotometer. The UV-Visible spectra were measured in DMF using Shimadzu UV-Vis. 160 A spectrophotometer in the range (200–1000) nm. Magnetic susceptibility measurement for complexes was obtained at room temperature using (magnetic susceptibility balance model MSB-MKI). Flame atomic absorption of elemental analyzer, shimadzu AA-670, was used for metal determination. Elemental microanalysis, was carried out using C.H.N.S elemental analyzer model 5500-Carlo Erba instrument. Gallen Kamp M.F.B.600.010 F. Melting point apparatus was used to measure the melting point of all the prepared compounds.

2.2 General Preparing of the Mixed Ligands Metal Complexes^[21,22]:

A ethanolic solution (10 ml) of the appropriate $\text{MCl}_2 \cdot \text{X}_2\text{O}$ (5mmol), is added to a ethanolic solution (20 ml) of equimolar (5mmoles) of the primary ligand aspirin (acetylsalicylic acid) (or paracetamol) and secondary ligand methyldopa . The reaction mixture is added gradually to the 0.5M of KOH solution, and the result mixture is heated for two hours. Cool the product mixture and the precipitate which is formed is filtrated and washed with 20 ml. of water then 20 ml. of ether. The result complex is dried in the oven at 70°C.

Table 1: The percentage weight of metals and ligands

No	Complexes	MCl ₂ .XH ₂ O	Asp	Meth	Para
1	[Mn(Asp)(Meth)(H ₂ O) ₂]	0.625gm	0.9gm	1.055gm	-----
2	[Fe(Asp)(Meth)(H ₂ O) ₂]	0.63gm	0.9gm	1.055gm	-----
3	[Co(Asp)(Meth)(H ₂ O) ₂]	1.19gm	0.9gm	1.055gm	-----
4	[Ni(Asp)(Meth)(H ₂ O) ₂]	1.185gm	0.9gm	1.055gm	-----
5	[Cu(Asp)(Meth)(H ₂ O) ₂]	0.85gm	0.9gm	1.055gm	-----
6	[Mn(Para)(Meth)(H ₂ O) ₂]	0.625gm	-----	1.055gm	0.755gm
7	[Fe(Para)(Meth)(H ₂ O) ₂]	0.63gm	-----	1.055gm	0.755gm
8	[Co(Para)(Meth)(H ₂ O) ₂]	1.19gm	-----	1.055gm	0.755gm
9	[Ni(Para)(Meth)(H ₂ O) ₂]	1.185gm	-----	1.055gm	0.755gm
10	[Cu(Para)(Meth)(H ₂ O) ₂]	0.85gm	-----	1.055gm	0.755gm

Meth=Methyldopa , Asp=Aspirin , Para=Paracetamol

3-Result and Discussion:

Tables (2-6) show the results of the conductivity data, IR spectroscopic, electronic spectra, magnetic moment data , metals% , CHNS and physical properties of complexes.

All the complexes were found to be stable, the stability of a chelate complexes depends on the size of the chelate rings, thus these ligands with a flexible organic backbone and their complexes contain five and six membered chelate rings, which have almost no strain.

The molar conductance data for the metal complexes in DMF

show non-electrolytic behavior in this solvent.

The brown color is overwhelmed all synthesized complexes. This color is obtained from the metal ions especially for iron (II) complexes (d 5) due to charge transfer from ligand to metal and vice versa.

The complexes were found to have M L1 L2.2H₂O, (M= divalent Manganese , Iron, Cobalt, Nickel, or Copper), (L1= Aspirin (acetylsalicylic acid) or Paracetamol, L2= Methyldopa) composition as indicate by elemental analysis that shown in Table (2)

Because of all three biomolecule ligands (aspirin (acetylsalicylic acid), paracetamol and methyldopa) are bidentate ligands, it forms two bonds with metal ion (central atom), thus water forms a complex with these metal ions, and owing to its

monodentate nature, it is not a chelating ligand as shown in Scheme (1 and 2)^[23].

At the same time the chelating effect phenomenon of dentate cheater of ligand provides bonding strength to the metal ion (central atom), and as the number of dentate increased, the tightness also increased^[23].

Table 2: Conductivity data of the complexes

No	Complexes	Conductivity in DMF Ω ⁻¹ cm ² mol ⁻¹
1	[Mn(Asp)(Meth)(H ₂ O) ₂]	20
2	[Fe(Asp)(Meth)(H ₂ O) ₂]	18
3	[Co(Asp)(Meth)(H ₂ O) ₂]	25
4	[Ni(Asp)(Meth)(H ₂ O) ₂]	17
5	[Cu(Asp)(Meth)(H ₂ O) ₂]	26
6	[Mn(Para)(Meth)(H ₂ O) ₂]	21
7	[Fe(Para)(Meth)(H ₂ O) ₂]	20
8	[Co(Para)(Meth)(H ₂ O) ₂]	24
9	[Ni(Para)(Meth)(H ₂ O) ₂]	19
10	[Cu(Para)(Meth)(H ₂ O) ₂]	25

3.1- IR spectra of the complexes:

Aspirin (acetylsalicylic acid) ligand spectrum shows bands at 1304, 1679 cm⁻¹ which may be assigned to (C-N) and cyano group (C=N) groups respectively^[24,25]. The band of (C-O) appeared at

1182 cm⁻¹ and symmetric (CO₂) group show at 1385 cm⁻¹. While paracetamol ligand shows 1290 cm⁻¹, 1654 cm⁻¹, 1171 cm⁻¹ and 1370 cm⁻¹ respectively^[26,27].

Finally, methylidopa spectrum shown 1288 cm⁻¹, 1663 cm⁻¹, 1170 cm⁻¹ and 1378 cm⁻¹ respectively^[28]. These bands of active groups for ligand are shifted to lower frequency after coordinate with metal as shown in the Table (3).

Table 3: IR spectra data of the complexes

No	Compounds	M-O	M-N	M-OH ₂	C-N	C=N	C-O	Sym CO ₂	Asym CO ₂
1	Aspirin (acetylsalicylic acid)	-----	-----	-----	1304 s	1679 m	1182 s	1385 m	1627 w
2	Paracetamol	-----	-----	-----	1290 s	1654 m	1171 s	-----	-----
3	Methylidopa	-----	-----	-----	1288 s	1663 m	1178 s	1378 m	1621 w
4	[Mn(Asp)(Meth)(H ₂ O) ₂]	624 m ,680 m	433 m ,462 m	734 m	1240 s	-----	1166 s	1325 m	1572 w
5	[Fe(Asp)(Meth)(H ₂ O) ₂]	621 m ,674 m	431 m ,460 m	680 m	1233s	-----	1163 s	1328 m	1597 w
6	[Co(Asp)(Meth)(H ₂ O) ₂]	626 m ,673 m	435 m ,460 m	724 m	1230 s	-----	1157 s	1323 m	1613 w
7	[Ni(Asp)(Meth)(H ₂ O) ₂]	623 m ,681m	438 m ,469 m	690 m	1237 s	-----	1158 s	1330 m	1605 w
8	[Cu(Asp)(Meth)(H ₂ O) ₂]	625 m, 676 m	433 m ,465 m	710 m	1239 s	-----	1110 s	1333 m	1600 w
9	[Mn(Para)(Meth)(H ₂ O) ₂]	615 m ,688 m	433 m ,478 m	727 m	1232 s	1606 m	1105 s	1323 m	1610 w
10	[Fe(Para)(Meth)(H ₂ O) ₂]	618 m ,890 m	435 m ,475 m	743 m	1239 s	1620 m	1108 s	1320 m	1616 w
11	[Co(Para)(Meth)(H ₂ O) ₂]	614 m ,683 m	438 m ,472 m	735 m	1220 s	1610 m	1120 s	1324 m	1609 w
12	[Ni(Para)(Meth)(H ₂ O) ₂]	620 m ,689 m	436 m ,475 m	780 m	1225 s	1613 m	1116 s	1322 m	1622 w
13	[Cu(Para)(Meth)(H ₂ O) ₂]	616 m ,684 m	431 m ,472 m	766 m	1230 s	1610 m	1123 s	1328 m	1604 w

Meth=Methylidopa

Asp=Aspirin

Para=Paracetamol

3.2- Electronic spectra of the complexes:

Three spin allowed transition to observe in low spin state for Mn(II) $\nu_1 = 12575, 12567.31 \text{ cm}^{-1}$, $\nu_2 = 29940.12, 29960.32 \text{ cm}^{-1}$ and $\nu_3 = 25150.01, 25120.88 \text{ cm}^{-1}$ also another four metals (divalent Iron, Cobalt, Nickel, and Copper) show three bands Table (4), these complexes exhibit six-coordinate octahedral geometry^[29,30].

3.3-Magnetic Susceptibility measurements:

The magnetic properties of the complexes provide valuable information for distinguishing their stereochemistry. The magnetic moments are

measured at 25°C. The magnetic moments for Mn(II) complexes (1&6) are (1.75,1.78) B.M, while for Fe(II) complexes (2&7) are (Zero)B.M. , for Co(II) complexes (3&8) are (1.86,1.85) B.M, while for Ni(II) complexes (4&9) are (2.81,2.80) and for Cu(II) complexes (5&10) are (1.91,1.85) B.M. These suggest the presence of one unpaired electron in the complexes of Mn(II),Co(II),Cu(II) and Suggest the presence of two unpaired electron in the complexes of Ni(II),while the complexes of Fe(II) are diamagnetic; confirming a low spin octahedral geometries.

Table 4 : Electronic spectra data for complexes

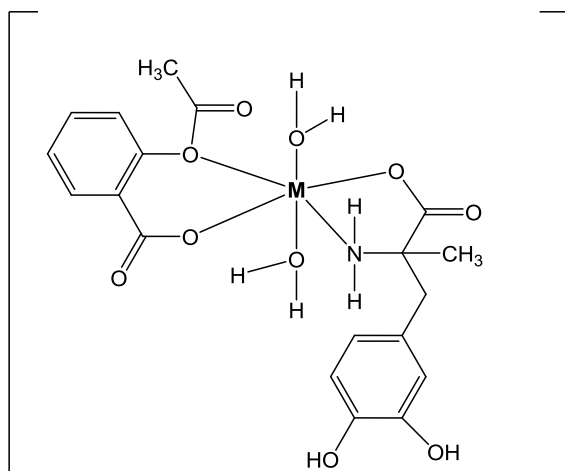
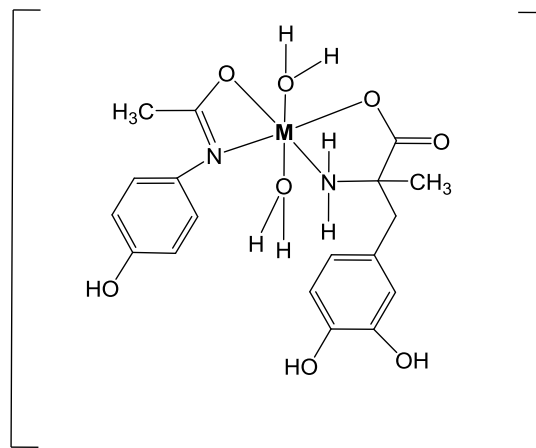
No	Complexes	$\nu_1 \text{ cm}^{-1}$	$\nu_2 \text{ cm}^{-1}$	$\nu_3 \text{ cm}^{-1}$
1	[Mn(Asp)(Meth)(H ₂ O) ₂]	12575.00	29940.12	25150.01
2	[Fe(Asp)(Meth)(H ₂ O) ₂]	19930.00	31446.54	39860.00
3	[Co(Asp)(Meth)(H ₂ O) ₂]	7751.99	16666.67	23364.48
4	[Ni(Asp)(Meth)(H ₂ O) ₂]	10183.29	11135.85	26666.67
5	[Cu(Asp)(Meth)(H ₂ O) ₂]	10000.00	12500.00	2427.84
6	[Mn(Para)(Meth)(H ₂ O) ₂]	12567.31	29960.32	25120.88
7	[Fe(Para)(Meth)(H ₂ O) ₂]	19960.58	31440.67	39880.88
8	[Co(Para)(Meth)(H ₂ O) ₂]	7776.32	16659.83	23358.73
9	[Ni(Para)(Meth)(H ₂ O) ₂]	19163.24	11153.82	26670.14
10	[Cu(Para)(Meth)(H ₂ O) ₂]	10183.30	14285.71	24038.46

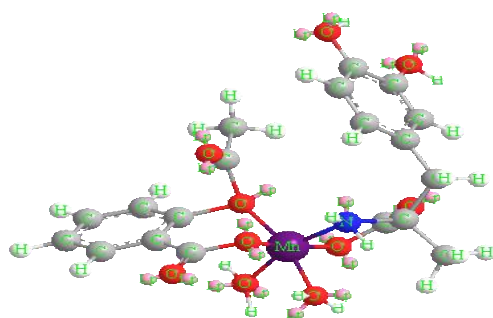
Table 5: Magnetic moment data for complexes

No	Complexes	μ_{eff} (theoretical)	μ_{eff} (practical)	$\chi_A \times 10^{-6}$ (e.g.s.u)	$\chi_m \times 10^{-6}$ (e.g.s.u)	$\chi_g \times 10^{-6}$ (e.g.s.u)
1	[Mn(Asp)(Meth)(H ₂ O) ₂]	1.73	1.75	1181.11	886.09	1.38
2	[Fe(Asp)(Meth)(H ₂ O) ₂]	0	0	0	0	0
3	[Co(Asp)(Meth)(H ₂ O) ₂]	1.73	1.86	1157.12	917.08	1.66
4	[Ni(Asp)(Meth)(H ₂ O) ₂]	2.83	2.81	3605.59	3329.56	4.92
5	[Cu(Asp)(Meth)(H ₂ O) ₂]	1.73	1.91	1055.85	815.81	1.47
6	[Mn(Para)(Meth)(H ₂ O) ₂]	1.73	1.78	1163.74	857.12	1.25
7	[Fe(Para)(Meth)(H ₂ O) ₂]	0	0	0	0	0
8	[Co(Para)(Meth)(H ₂ O) ₂]	1.73	1.85	1145.23	902.17	1.62
9	[Ni(Para)(Meth)(H ₂ O) ₂]	2.83	2.80	3573.96	3254.61	4.87
10	[Cu(Para)(Meth)(H ₂ O) ₂]	1.73	1.85	1043.71	801.26	1.41

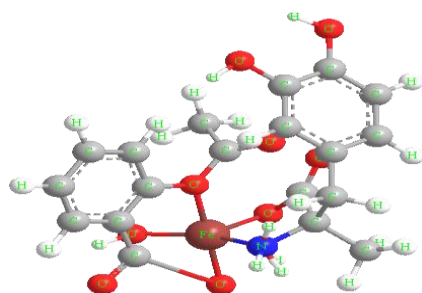
Table 6 : Metals% , CHNS and physical properties of complexes

No	Molecular weight	Color	m.p	%C	%H	%N	%M
				Theoretical (Practical)	Theoretical (Practical)	Theoretical (Practical)	Theoretical (Practical)
1	443.94	Dark Brown	250d	51.36 (51.44)	4.28 (4.25)	3.15 (3.18)	12.38 (12.32)
2	444.85	Brown	262d	51.25 (51.30)	4.27 (4.25)	3.15 (3.17)	12.58 (12.61)
3	447.93	Light Brown	240d	50.90 (50.75)	4.24 (4.21)	3.13 (3.14)	13.16 (13.20)
4	447.69	Brown	270d	50.93 (50.79)	4.25 (4.23)	3.13 (3.15)	13.11 (13.10)
5	452.54	Dark brown	265d	50.38 (50.20)	4.20 (4.18)	3.10 (3.06)	14.04 (14.00)
6	414.94	Light Brown	250d	52.10 (52.20)	4.20 (4.18)	6.75 (6.66)	13.24 (13.26)
7	415.85	Brown	254d	51.94 (52.31)	4.81 (4.73)	6.73 (6.69)	13.43 (13.38)
8	418.93	Brown	266d	57.29 (57.10)	4.75 (4.71)	6.68 (6.62)	14.07 (14.12)
9	418.69	Light Brown	263d	57.32 (57.43)	4.78 (4.71)	6.69 (6.65)	14.02 (14.08)
10	423.54	Dark brown	270d	56.67 (56.73)	4.72 (4.74)	6.61 (6.58)	15.00 (15.12)

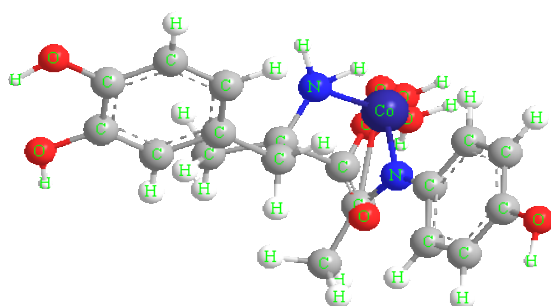
d = decomposed**Scheme (1):****The chemical structure of complexes (1-5)****M= Mn(II), Fe(II), Co(II), Ni(II) and Cu(II)****Scheme (2):****The chemical structure of complexes (6-10)****M= Mn(II), Fe(II), Co(II), Ni(II) and Cu(II)**



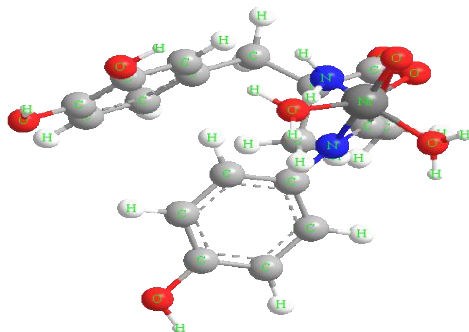
Scheme (3): The 3D chemical structure of [Mn(Asp)(Meth)(H₂O)₂]



Scheme (4): The 3D chemical structure of [Fe(Asp)(Meth)(H₂O)₂]



Scheme (5): The 3D chemical structure of [Co(Para)(Meth)(H₂O)₂]



Scheme (6): The 3D chemical structure of [Ni(Para)(Meth)(H₂O)₂]

Conclusion:

The methods for preparation of these mixed complexes were suitable for all metals used in this work, and these ten new complexes (1-10) of the two mixed ligands have been found to act as bidentate chelating agents, and coordinate through the oxygen of Aspirin (acetylsalicylic acid)'s ester group and oxygen of the carboxyl group, while Methyldopa complexes coordinate through the oxygen of the carboxyl group and the nitrogen of the amide groups. The Paracetamol was coordinated through the oxygen atom of carboxyl group and the nitrogen atom of the amide group.

These mixed ligands were flexible organic backbone and their complexes contain five and six membered chelate rings, which have almost no strain. The molar conductance data for the metal complexes show non-electrolytic behavior in DMF solvent.

The all synthesized complexes which show non-electrolytic properties, also were no conducting electrical current behaved as bi-dentate with octahedral geometrical isomers.

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References:

- [1] Salem, W. M. (2019). Sensitive determination of Paracetamol using Ferrocene Nanoparticles by Chitosan-Functionalized-Modified Carbon Past Electrode. *Egyptian Journal of Chemistry*, 62(4), 679-690.
- [2] Zayed, M. A., El-Dien, F. N., Mohammed, G. G., & El-Nahas, R. E. (2005). Spectrophotometric assay of levodopa and alpha-methyldopa in pharmaceutical products and in biological samples of schizophrenic patients using copper complex and tri-iodide reagent. *Egyptian Journal of Chemistry*, 48(4), 437.
- [3] Patil, S. S., Thakur, G. A., & Shaikh, M. M. (2011). Synthesis, Characterization, and Antibacterial Studies of Mixed Ligand Dioxouranium Complexes with 8-Hydroxyquinoline and Some Amino Acids. *Isrn Pharmaceutics*, 2011.
- [4] Aldahham, B. J., Al-Khafaji, K., Saleh, M. Y., Abdelhakem, A. M., Alanazi, A. M., & Islam, M.

- A. (2020). Identification of naphthyridine and quinoline derivatives as potential Nsp16-Nsp10 inhibitors: a pharmacoinformatics study. *Journal of Biomolecular Structure and Dynamics*, 1-8.
- [5] Davies, D. B., Veselkov, D. A., Djimant, L. N., & Veselkov, A. N. (2001). Hetero-association of caffeine and aromatic drugs and their competitive binding with a DNA oligomer. *European Biophysics Journal*, 30(5), 354-366.
- [6] El-Sherif, A. A. (2010). Mixed ligand complex formation reactions and equilibrium studies of Cu (II) with bidentate heterocyclic alcohol (N, O) and some bio-relevant ligands. *Journal of solution chemistry*, 39(1), 131-150.
- [7] Ali, H. A., Fares, H., Darawsheh, M., Rappocciolo, E., Akkawi, M., & Jaber, S. (2015). Synthesis, characterization and biological activity of new mixed ligand complexes of Zn (II) naproxen with nitrogen based ligands. *European Journal of Medicinal Chemistry*, 89, 67-76.
- [8] Okasha, R. M., Al-Shaikh, N. E., Aljohani, F. S., Naqvi, A., & Ismail, E. H. (2019). Design of Novel Oligomeric Mixed Ligand Complexes: Preparation, Biological Applications and the First Example of Their Nanosized Scale. *International journal of molecular sciences*, 20(3), 743.
- [9] Woertink, J. S., Tian, L., Maiti, D., Lucas, H. R., Himes, R. A., Karlin, K. D., ... & Solomon, E. I. (2010). Spectroscopic and computational studies of an end-on bound superoxo-Cu (II) complex: geometric and electronic factors that determine the ground state. *Inorganic chemistry*, 49(20), 9450-9459.
- [10] Mauri, L., Kereiakes, D. J., Yeh, R. W., Driscoll-Shempp, P., Cutlip, D. E., Steg, P. G., ... & Massaro, J. M. (2014). Twelve or 30 months of dual antiplatelet therapy after drug-eluting stents. *New England Journal of Medicine*, 371(23), 2155-2166.
- [11] Miesbach, W., & Seifried, E. (2012). New direct oral anticoagulants—current therapeutic options and treatment recommendations for bleeding complications. *Thrombosis and haemostasis*, 108(10), 625-632.
- [12] Stergiakouli, E., Thapar, A., & Smith, G. D. (2016). Association of acetaminophen use during pregnancy with behavioral problems in childhood: evidence against confounding. *JAMA pediatrics*, 170(10), 964-970.
- [13] Pickering, G., Macian, N., Libert, F., Cardot, J. M., Coissard, S., Perovitch, P., ... & Dubray, C. (2014). Buccal acetaminophen provides fast analgesia: two randomized clinical trials in healthy volunteers. *Drug design, development and therapy*, 8, 1621.
- [14] Al-Obidi, L. K., & Al-Noor, T. H. (2018). Synthesis, Spectral and Bacterial Studies of Mixed Ligand Complexes of Schiff Base Derived from Methyl dopa and Anthranilic Acid with Some Metal Ions. *Ibn AL-Haitham Journal For Pure and Applied Science*, 235-247.
- [15] Beale, J. M., Block, J., & Hill, R. (2010).; Wilson and Gisvoled Text Book of Organic Medicinal and Pharmaceutical Chemistry " The Analgesic Antipyretics Acetaminophen (Paracetamol) and Related Analogs " Organic medicinal and pharmaceutical chemistry, Chapter 24 (Analgesics), p803-804 ; 12th Edition.; Wolters Kluwer, Lippincott Williams and Wilkins New York. London
- [16] Renfrew, A. K. (2014). Transition metal complexes with bioactive ligands: mechanisms for selective ligand release and applications for drug delivery. *Metallomics*, 6(8), 1324-1335.
- [17] Weder, J. E., Dillon, C. T., Hambly, T. W., Kennedy, B. J., Lay, P. A., Biffin, J. R., ... & Davies, N. M. (2002). Copper complexes of non-steroidal anti-inflammatory drugs: an opportunity yet to be realized. *Coordination Chemistry Reviews*, 232(1-2), 95-126.
- [18] Kalia, S. B., Kaushal, G., Kumar, M., Cameotra, S. S., Sharma, A., Verma, M. L., & Kanwar, S. S. (2009). Antimicrobial and toxicological studies of some metal complexes of 4-methylpiperazine-1-carbodithioate and phenanthroline mixed ligands. *Brazilian Journal of Microbiology*, 40(4), 916-922.
- [19] Siddiqi, Z. A., Khalid, M., Kumar, S., Shahid, M., & Noor, S. (2010). Antimicrobial and SOD activities of novel transition metal complexes of pyridine-2, 6-dicarboxylic acid containing 4-picoline as auxiliary ligand. *European journal of medicinal chemistry*, 45(1), 264-269.
- [20] Patel, K. S., Patel, J. C., Dholariya, H. R., Patel, V. K., & Patel, K. D. (2012). Synthesis of Cu (II),

- Ni (II), Co (II), and Mn (II) complexes with ciprofloxacin and their evaluation of antimicrobial, antioxidant and anti-tubercular activity.
- [21] Abbas, A. M., Mohammed Taib, A. S., & Saeed, N. H. (2020). Synthesis and Characterization of Linear Thermally Stable polyester contain Schiff Bases. *Egyptian Journal of Chemistry*, 63(8), 45-52.
- [22] BICHAN, M. J. K., & ABDOON, F. M. (2019). A NOVEL SPECTROPHOTOMETRIC DETERMINATION OF METHYLDOPA THROUGH TERNARY COMPLEXATION PROCEDURE USING FE (III), MN (II), AND CO (II) WITH 2-AMINOPYRIDINE. *Asian Journal of pharmaceutical and Clinical Research*.
- [23] Singh, J., Srivastav, A. N., Singh, N., & Singh, A. (2019). Stability Constants of Metal Complexes in Solution. In *Stability of Coordination Compounds*. IntechOpen.
- [24] Dawood, Z. F., & Al-Moula, F. J. A. (2010). New Mixed Ligand Complexes of Co (II) & Ni (II) Containing Isatinazine and Semicarbazone. *Iraqi National Journal Of Chemistry*, (38), 349-360.
- [25] Saleh, M., Ayoub, A. I., & Hammady, A. O. (2020). Synthesis biological studies of some new heterocyclic compound derived from 2-chloro-3-formyl quinoline and 4-(benzyl sulfonyl) acetophenone. *Egyptian Journal of Chemistry*, 63(12), 4769-4776.
- [26] Sunatsuki, Y., Fujita, K., Maruyama, H., Suzuki, T., Ishida, H., Kojima, M., & Glaser, R. (2014). Chiral crystal structure of a P 212121 kryptoracemate iron (II) complex with an unsymmetric azine ligand and the observation of chiral single crystal circular dichroism. *Crystal growth & design*, 14(8), 3692-3695.
- [27] Guru, P. (2009). Studies of two Complexes with Ampicillin. *Int. J. of Chem. Tech. Research*, 1(3), 461-463.
- [28] W Ibrahim, M., & F Dawood, Z. (2006). Preparation and Study of Some Binuclear Nickel (II) Complexes Containing Mixed Ligands (Salicylaldehyde Thiosemicarbazone and Carboxylic Acid). *Rafidain Journal of Science*, 17(4), 8-17. M. N. Patel Ibrahim (2002)"preparation of Co II and Ni II complexes contain mixed ligands and their radiolytical study". M. Sc. Thesis, 2002, Mosul Univ . Edu. College Chem. Dept.
- [29] IBRAHIM, M., & DAWOOD, Z. (2005). Radiolysis of Cobalt (II) and Nickel (II)-Complexes Containing Mixed Ligands by Gamma Rays. *Iraqi National Journal Of Chemistry*, (20), 547-558.
- [30] Wilkinson, G., Gillard, R. D., & McCleverty, J. A. 1987Comprehensive coordination chemistry.

تحضير معقدات جديدة من خليط الاسبرين والباراسيتامول والمثيل دوبا مع المنغنيز, (II) الحديد, (II) الكوبلت, (II) النيكل (II) والنحاس (II) مع دراسة الخصائص الفيزيائية والكيميائية.

الملخص:

تم تحضير معقدات جديدة من خلأاط الاسبرين مع مثيل دوبا أو الباراسيتامول مع مثيل دوبا عن طريق تصعيد خليط التفاعل باستخدام وسط قاعدي لسحب البروتونات من هذه الليكندات, وقد درست خصائص المعقدات الجديدة المحضرة للمنغنيز, (II) الحديد, (II) الكوبلت, (II) النيكل (II) والنحاس (II) باستخدام اطياف الأشعة تحت الحمراء و فوق البنفسجية- المرئية, المغناطيسية, الامتصاص الذري للهب, التحليل الدقيق للعناصر وقياسات درجة الانصهار. وجد ان الليكندات المختلطة المستخدمة تسلك سلوك ليكندات مخلبية ثنائية السن حيث ترتبط معقدات الاسبرين مع الايون الفلزي من خلال ذرات اوكسجين الاستر واوكسجين المجموعة الكربوكسيلية, اما في جزيئة المثيل دوبا فتم الارتباط باستخدام ذرة الاوكسجين لمجموعة الكاربوكسيل و نتروجين مجموعة الاميد بينما ارتبطت جزيئة الباراسيتامول بذرة اوكسجين المجموعة الكربوكسيلية وذرة نتروجين قاعدة شيف المتكونة.