Iraqi National Journal of Chemistry

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Preparation of New Complexes of Anticipated Biological Activities

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Abstract:

Novel complexes of biological important activity were prepared by coordination of Mn(II) or Cr(II) metals with the ligand of Aspirin and Paracetamole mixture
L = Aspirine(Asp) and Paracetamole(Parac) in 1:1:1 for the former and 1:1:2 molar ratio for the later.
The metal ions were tetrahedral and octahedral bonded to the ligand in the complexes respectively. Aspirin coordinate through the carbonyl oxygen of the carboxyl and the ester groups, while paracetamol coordinate through the oxygen of the hydroxyl and the
amide groups Complexes have been synthesized by conventional direct reaction in neutral medium and the products have the general formula $[M(Asp/\ Par]Cl_2$and $[M_2(Asp)_2/\ (Par)_2]Cl_2$ respectively.
Physical measurements including IR and UV / Visible spectra, CHN analysis and molar conductivity measurements showed these geometries around the metals. The geometry (three dimensional structure) of complex (I and V) as representative of these complexes at minimized energy was established by chem.3D Ultra; molecular modeling and analysis confirmed the suggested structure tetrahedral and octahedral.

Keywords:

Aspirine(Asp) and Paracetamole(Par) mixture, Mn and Cr transition Metal complexes.

تحضير معقدات جديدة يتوقع ان يكون لها فعاليات بايلوجية

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الملخص:

تم تحضير معقدات فلزات العناصر الانتقالية المنغنيز,والكروم والتى يتوقع لها فعالية بيولوجية بوساطة تناسق فلز المنغنيز والكروم مع ليكاند خليط من الاسبرين والباراسيتامول بنسبة مولارية1:1:1 واخرى 2:1:1. على التوالى وقد اعطت هذه الفلزات معقدات رباعية وثمانية السطوح على التوالى .يتناسق الاسبرين من خلال اوكسجين مجموعة الكاربونيل ومجموعة الاستر فى حين يتناسق الباراسيتامول من خلال اوكسجين مجموعة الهيدروكسيل ومجموعة الاميد.حضرت هذه المعقدات بوساطة التفاعل التقليدي المباشر (بوسط متعادل) لاعطاء معقدات ذات الصيغة :
$[M(Asp)/(Par)]Cl_2$ و $[M_2(Asp)_2/(Par)_2]Cl_2$
على التوالي .
اعطت القياسات الفيزيائية والمتضمنة أطياف الأشعة تحت الحمراء وفوق البنفسجية – المرئية والتحليل الدقيق للعناصر اضافة الى التوصيلة الكهربائية المولارية معقدات رباعية بالنسبة للاول و ثمانية السطوح بالنسبة للاخر. اثبتت الاشكال المتوقعة بوساطة الشكل الثلاثى لهيئة المعقدين(I و V) كممثلا عن بقية المعقدات وبالطاقة الدنيا .

الكلمات المفتاحية:
اسبرين ، باراسيتامول، معقدات المغنيز والكروم الانتقالية

Introduction:

Aspirin (acetylsalicylic acid) Fig (1a), frequently used as an analgesic antipyretic to diminish fever, and as an anti-inflammatory treatment[1-4].

In 2007 Lawal and Obaleye reported the synthesis of new complexes of Co (II), Ni (II) and Fe (III) with aspirin and paracetamol [5].

Paracetamol, N-acetyl-p-aminophenol Fig(1b), is a widely used as weak anti-inflammatory activity[4]

Complexes derived from drug(s) and a variety of metal ions have often been studied because of their technical applications [6-7].

The studies of new transition metals complexes of Mn(II) or Cr(II) metals with the ligand of Aspirin and Paracetamole mixture of anticipated biological activity have been reported in present work .

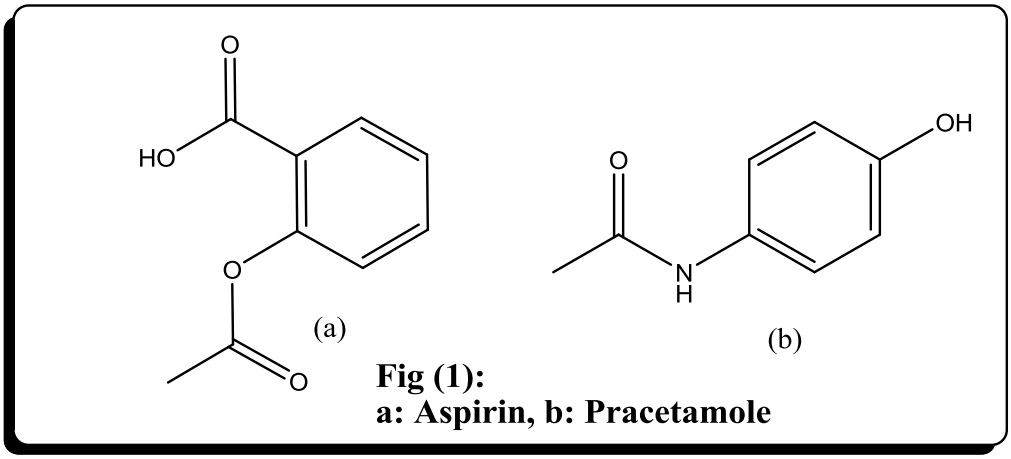


Fig (1):
a: Aspirin, b: Pracetamole

Experimental:

MATERIALS AND METHODS

Aspirin and Paracetamole were obtained from Alhukamaa Drug Industry(Mosul-Iraq). Physico-chemical analysis such as Solubility, Melting point and Conductivity measurement were carried out in Industrial Chemistry Department.

METHODOLOGY SYNTHESIS OF THE COMPLEXES:
SYNTHESIS OF [M(Asp/ Par]Cl_2] COMPLEXES[(1-II):[5]

Ethanolic solution of Aspirin (10mmole) and Paracetamole (10mmole) was added to a mixture of equimolar amounts(10mmole) of proper metal salt MCl_2(M = Mn(II) or Cr(II)). This result mixture was refluxed for 5 hours, cooled to r.t. and the solid product was filtered and then washed with ethyl alcohol , desiccated and purified by recrystallized from acetone. physical properties and spectral data of the complexes were listed in Table (1), while spectral data were listed in Table (2).

METHODOLOGY SYNTHESIS OF THE COMPLEXES:
SYNTHESIS OF [$M_2(Asp)_2$/ $(Par)_2$]Cl_2] COMPLEXES[(III-IV): [5]

Potassium hydroxide solution of (0.1M) was added to ethanolic solution of Aspirin (10mmol) then Paracetamole (10mmole) . Metal salts Mn(II) (5mmole) or Cr(II) (20mmole) were added to the mixture at pH (8-8.5),, and worked up as in the first method. physical properties and

spectral data of the complexes were listed in Table (1), while spectral data were listed in Table (2).

No.	Formula of Ligands/ complexes*	M.Wt	Color	Yield %	Elemental analysis %			Conductivity (Ohm^{-1} cm^2 mol^{-1})
					C	H	N	
					Found Calculated	Found Calculated	Found Calculated	
Asp	$C_9H_8O_4$	180	white	-	-	-	-	--
Par	$C_8H_9NO_2$	151	white	-	-	-	-	
I	$[Mn(Asp)(Par)]Cl_2$	457	pink	88	51.00 51.93	4.00 4.39	3.50 3.59	75
II	$[Cr(Asp)(Par)]Cl_2$	454	green	88	52.32 52.32	4.99 4.36	3.00 3.56	73
III	$[Mn_2(Asp)_2(Par)_2]Cl_2$	839	violet	86	45.44 45.57	3.09 3.82	3.10 3.31	76
IV	$[Cr_2(Asp)_2(Par)_2]Cl_2$	833	green	78	46.01 46.17	3.87 3.87	2.90 3.17	78
V	$[MnCr(Asp)_2(Par)_2]Cl_2$	836	green	69	45.8 45.87	3.00 3.85	2.90 3.15	77

*All these complexes were decomposed over 300^0C .

Table (2): spectral data of ligand and the complexes(I-V).

METHODOLOGY SYNTHESIS OF THE COMPLEXES:

SYNTHESIS OF $[M M'(Asp)_2/ (Par)_2]Cl_2$] COMPLEXES[(V):):[5]

Potassium hydroxide solution of (0.1M) was added to ethanolic solution of Aspirin (10mmol) then Paracetamole (10mmole) .The two metals salts Mn(II) (10mmole) and Cr(II) (10mmole) were added to the mixture at pH (8-8.5), and worked up as in the first method. physical properties and spectral data of the complexes were listed in Table (1), while spectral data were listed in Table (2).

Results and Discussion:

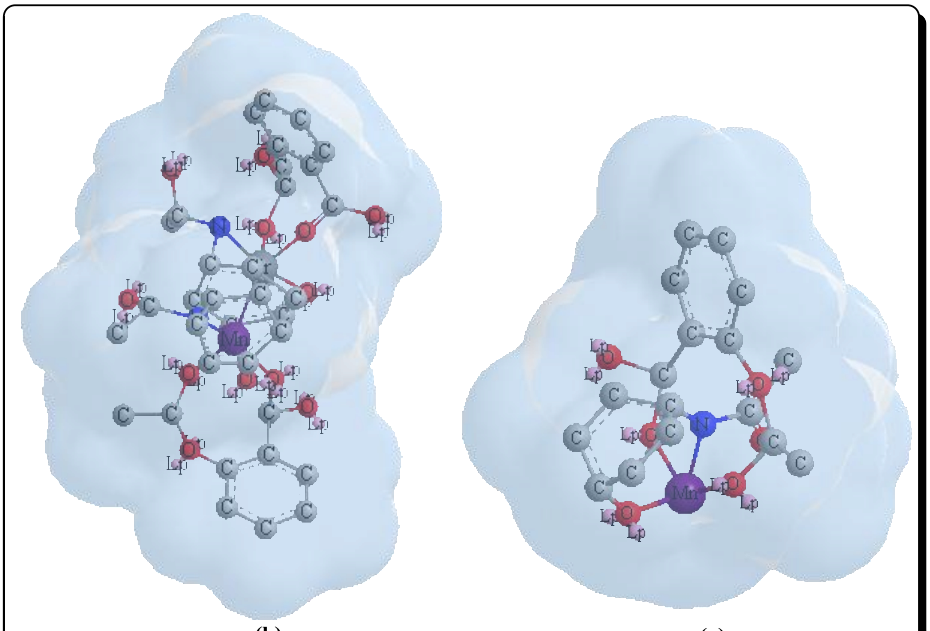
In this work the mixture of these two drugs were used together to coordinate with Cr(II) or/and Mn(II) as individual and as mixed ligands. To our knowledge this is the first time to synthesis these new complexes, and as the two drugs act against antibacterial we anticipated that those complexes also of biological activity.

Thus, these novel complexes were prepared by coordination of Mn(II) or/and Cr(II) metals with the ligand of Aspirin and Paracetamole mixture L = Aspirine(Asp) and Paracetamole(Parac) in 1:1:2 and 1:1:1 molar ratio .

These ions were tetrahedral (I-II) and octahedral (III-V) bonded to the ligand in the complexes. Aspirin coordinate through the oxygen of the C=O and the C-O-R groups, while paracetamol coordinate through the oxygen of OH and the amide groups .

These complexes have been synthesized by conservative undeviating reaction in (pH=7) medium and the products have the general formula $[M(Asp/ Par]Cl_2$ for (I-II) and $[M_2(Asp/ Par]Cl_2$ for (III-V) respectively.

Physical measurements confirmed the suggested structure Fig 2(a and b).



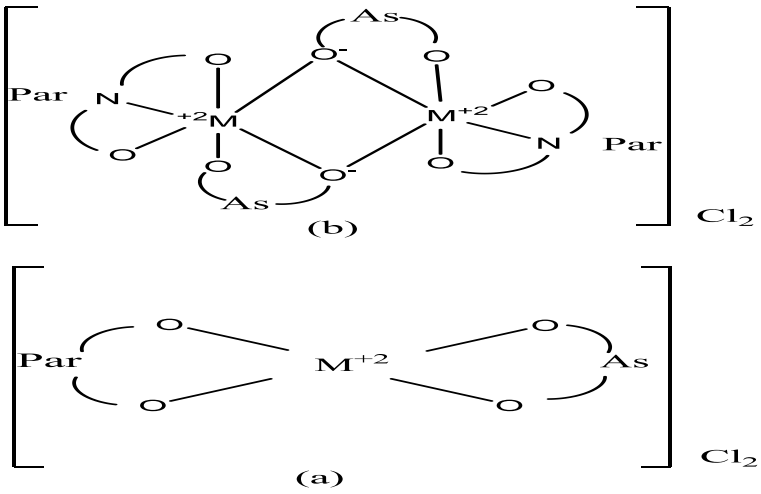
(b) (a)

Fig (2) a: Complexe (I), b: Complexe (V) drawn by ChemBioDraw 3d Ultra 2008 , as Ball and Stick , with minizing energy (MM2) and Model Display: Hydrogen atoms were hided

Also the molar formula of these complexes were proved by the IR and UV-Visible spectra in addition to molar conductivity. Table (1).

Uv spectra for these complexes Table (2) showed absorption bands from 291-640 these bands due to d-d transitions and indicated that these complexes were octahedral and tetrahedral geometry, Fig (3) was the UV spectra of complex (II) as a representative for these complexes [4]. Scheme (1) shows the proposed structures of complexes [M(Asp/ Par]Cl_2 and [$M_2(Asp)_2$/($Par)_2$]Cl_2 .

No.	μeff(B.M)	UV (EtOH) d-d transitions λ max	I.R (KBr) , υ cm^{-1}					
			C=O	NH	ph-OH	M-O	M-N	M-O
ligand			،1750،1675 1625	3690	3785	-	-	-
I	5.97	301	1560,1635, 1522	-	3232	-	-	472
II	5.12	291	1558,1618 1512	-	3342	-	-	472
III	5.96	304, 346,406	1601,1645, 1557	3627	3749	1401	418	574
IV	4.96	338,468,652	1645,1650, 1590	3700	3750	1391	440	452
V	-------	340,450,640	1620,1680, 1589	3644	3746	1420	420	563



Scheme (1):
The proposed structures of complexes
(a)(I-II) $[M(Asp/\ Par]Cl_2$ and
(b)(III-V)$[M_2(Asp/\ Par]Cl_2$
M = Mn(II), Cr(II)

The conductivity measurements in 10^{-3}M DMSO have indicated that these complexes behaved 1:2 electrolyte in this solvent [14-16].

A study of infrared spectra of metal complexes(Table2).In the IR spectrum of the complex(III-Fig4)a very strong band appeared at 1557-1645 cm^{-1}due to (C=O) bond which confirms the formation .Another band near 3627 cm^{-1}(NH) was found.The weak band due to O^- coordinate with metals ions were 1401 cm^{-1} . Finally،418 and 574 cm^{-1} for M-N and M-O respectively،while the IR of the complex (IV-Fig5)،a very strong band appeared at 1590 -1650 cm^{-1} due to (C=O) bond which confirms the formation.Another band near 3700 cm^{-1} (NH) was found.The weak band due to O^- coordinate with metals ions were 1391 cm^{-1}.Final-1ly،440 and 452 cm^{-1} for M-N and M-O respectivly.These results indicate the shifted of ligand frequencies to lower values.

The practical values of magnetic moment for complexes (I-II) were (5.97B.M) and (5.12B.M) respectively. These values were in agree whith the Mn(II) and Cr(II) tetrahedral complexes(4). While thatl values of magnetic moment for complexes (III-IV) were (5.96B.M) and (4.96B.M) respectively. These values were in agree whith the Mn(II) and Cr(II) octahedral.

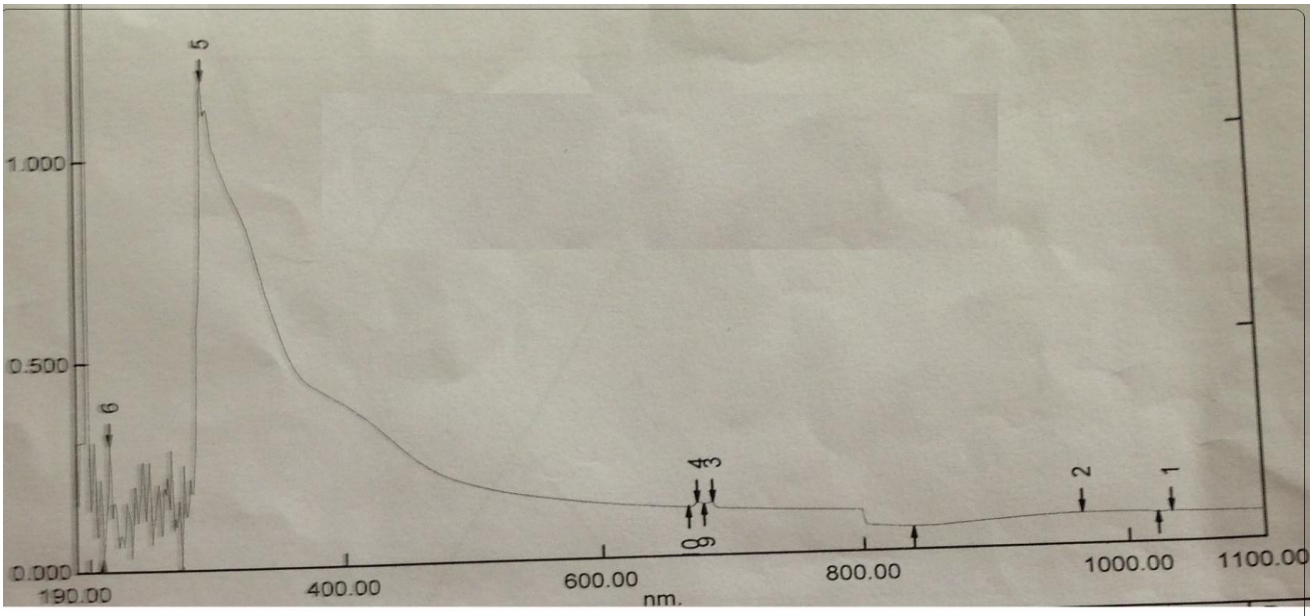


Fig (3) The UV spectra of complex (II)

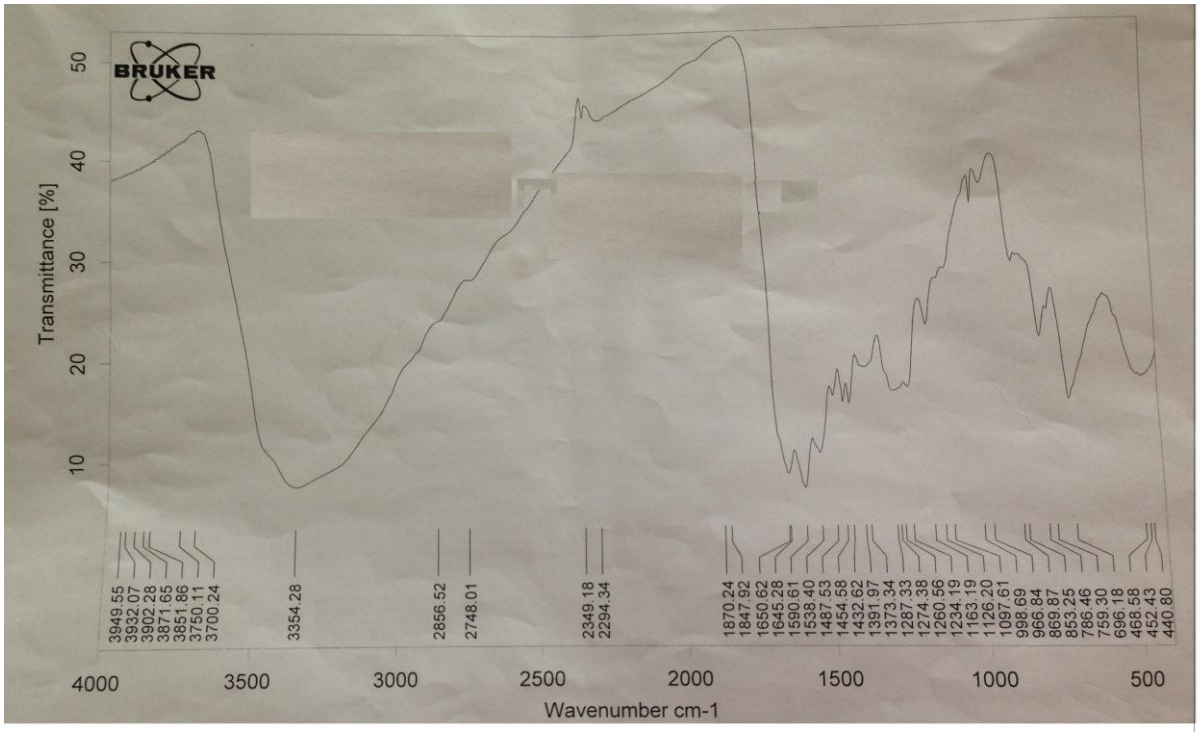


Fig (4) The IR spectrs of complex (III)

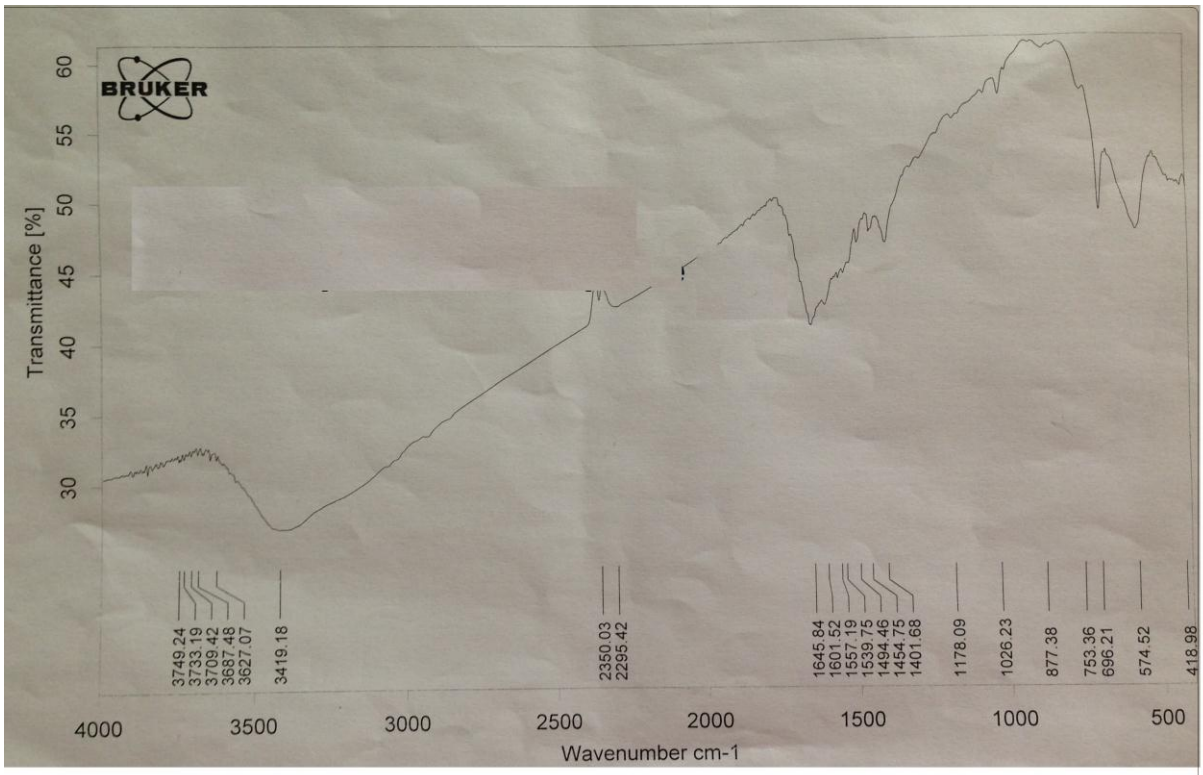


Fig (5): The IR spectra of complex (IV)

References:

1- W. Sneader," The discovery of aspirin: a reappraisal"BMJ. 321 (7276): (2000) 1591–1594].

2-H D Lewis,; J W Davis, D G Archibald, W E Steinke, T C Smitherman, J E Doherty, H W Schnaper, M M LeWinter, E Linares, J M Pouget, S C Sabharwal, E Chesler, H DeMots (1983). "Protective effects of aspirin against acute myocardial infarction and death in men with unstable angina. Results of a Veterans Administration Cooperative Study". The New England Journal of Medicine **309** (7): 396–403.

3- Krumholz, Harlan M.; Martha J. Radford, Edward F. Eller beck, John Hennen, Thomas P. Meehan, Marcia Petrillo, Yun Wang, Timothy F. Kresowik, Stephen F. Jencks (1995). "Aspirin in the Treatment of Acute Myocardial Infarction in Elderly Medicare Beneficiaries : Patterns of Use and Outcomes". Circulation **92** (10): 2841–2847.

4-Ammar Abd-Aljabar Aziz ; Preparation of New transition and non Transition metals complexes with N-acetylglucose amine(NAGA ; Iraqi National Journal of Chemistry; 2013 volume50 ,191198

5-A. Lawal and J. A. Obaleye" Synthesis, characterization and antibacterial activity of aspirin and paracetamolmetal complexes"; (2007); BIOKEMISTRI 19(1):9-15

6-N. Raman, V. Muthuraj, S. Ravichandran, and A. Kulandaisamy, “Synthesis, characterisation and electrochemical behaviour of Cu(II), Co(II), Ni(II) and Zn(II) complexes derived from acetylacetone and p-anisidine and their antimicrobial activity,” Journal of Chemical Sciences, vol. 115, no. 3, pp. 161–167, 2003.

7-C. Briickner, S. J. Rettig, and D. Dolphin, 2-Pyrrlythiones as monoanionic bidentate N, S-chelators: synthesis and molecular structure of 2-pyrrlythionato complexes of Ni(II), Co(II) and Hg(II),” Inorganic Chemistry, vol. 39, pp. 6100–6106, 2000.

8-M. K. Samota and G. Seth; (2010)" Synthesis, characterization, and antimicrobial activity of palladium(II) and platinum(II) complexes with 2-substituted benzoxazole ligands "; Heteroatom Chemistry; V 21, Issue 1; Pages 1–50

9-Scottish Intercollegiate Guidelines Network (SIGN) (2008). "6.1 and 7.1.1". Guideline 106: Control of pain in adults with cancer. Scotland: National Health Service (NHS). ISBN 978 1 905813 38 4] .