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Synthesis and Spectroscopic Studies of Some transition metal Complexes with Mixed ligand of Metformin and Cysteine

Basim I. Al-Abdali, Issam M. A. Shakir, Huda M. Nafea*
Department of Chemistry, College of Science, University of Baghdad, Baghdad, Iraq

Abstract

Mixed ligand complexes of Cu(II), Ni(II) and Co(II) with metformin(MTF) as primary ligand and cysteine(Cys) as secondary ligand have been prepared and characterized by elemental analysis, atomic absorption, molar conductivity, magnetic susceptibility measurements, FTIR,UV-Vis ,^{1}H-NMR and ^{13}C-NMR spectral studies. The elemental analysis, atomic absorption data reveal the formation of [1:1:1] [M:MTF:Cys] complexes.The electronic spectra and magnetic moment measurements reveal the presence of complexes in an octahedral geometry and the molar conductivity studies of the complexes indicate their non-electrolytic nature. The infrared and NMR spectral were showed that the chelation behaviour of the ligands towards selected transition metal ions are through two imino groups of MTF and the sulphur atom and the amino nitrogen of cysteine.

Keywords: Mixed ligands complexes; divalent complexes of Cu, Ni and Co; metformin; cysteine.

تحضير ودراسات طيفية لمعقدات بعض العناصر الانتقالية مع مزيج ليكندي من الميتفورمين والسيستئين

باسم ابراهيم العبدلي، عصام محمد علي شاكر، هدى مؤيد نافع*
قسم الكيمياء، كلية العلوم، جامعة بغداد، بغداد، العراق

الخلاصة

حضرت معقدات مخلبية لايون النحاس االثنائي، النيكل الثنائي والكوبلت الثنائي من مزيج ليكندي أستخدم فيه عقار الميتفورمين كليكند أساسي ومادة السيستئين كليكند ثانوي وشخصت هذه المعقدات بواسطة تحاليل العناصر ، الامتصاص الذري ، أطياف الاشعة تحت الحمراء، الرنين المغناطيسي النووي، الاطياف الالكترونية، التوصيلية المولارية وقياسات الحساسية المغناطيسية . إن تحاليل العناصر وبيانات الامتصاص الذري أظهرت تكوين المعقدات بنسبة مولية مساوية الى [1:1:1] [M:MTF:Cys] بينما أظهرت قياسات العزم المغناطيسي والاطياف الالكترونية تواجد المعقدات بهيئة تناسق هندسي ثماني السطوح . اضافة الى ذلك أشارت دراسات التوصيلية المولارية الطبيعة الغير موصلة للمعقدات في حين إن بيانات طيف الاشعة تحت الحمراء و الرنين المغناطيسي النووي أظهرت السلوك المخلبي لمزيج الليكندين نحو ايونات الفلزات الانتقالية المختارة من خلال مجموعتي الإمينو لعقار الميتفورمين أما بالنسبة للحامض الاميني(السيستئين) فكان من خلال ذرة الكبريت وذرة النتروجين لمجموعة الأمينو.

Introduction

Among the various substituted biguanides, Metformin.HCl (MTF.HCl; N,N-dimethyl biguanide hydrochloride) [1] is one of the interesting compounds that chelate metals.

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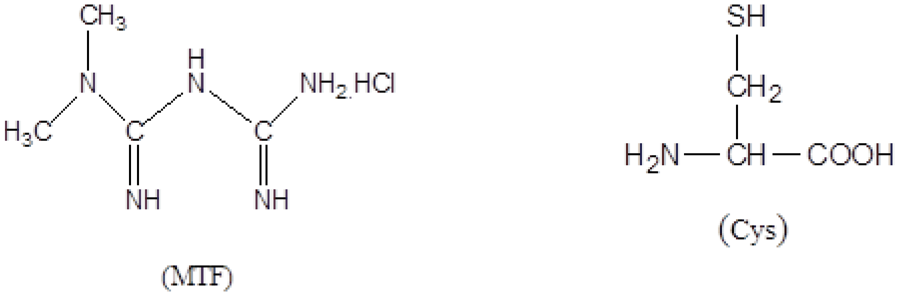
*Email: mhuda555@yahoo.com

It is an antidiabetic agent which uses in the treatment of non-insulin- dependent diabetes mellitus (NIDDM)[2,3] , it also acts as antimicrobial, analgesic, antimalerial [4] and antimetabolite for organisms that inhibit the metabolism of folic acid [5]. Recently, it was found that vanadyl complex with metformin shows potential synergistic insulin mimics [6], while platinum (IV) complex reveals antitumor activity [7].

The other metformin complexes like Co(II) [8], Zn(II) [9] and Pt(II) [10] complexes possess antimicrobial activity and also have an interesting thermal behavior [11]. Studies have shown that cysteine may be considered a biologically important ligand manifested in the formation of chelate rings involving various coordination (N,S; O,S; or N,O) site [12,13]. In view of its biological and chemical properties, cysteine is a suitable ligand for the synthesis of complexes involving bioactive metals as cobalt, nickel and copper [14,15]. Cysteine has been used as a co-ligand to form mixed ligand complexes of ranitidine which is the most usful drug in the management of peptic and duodenal ulcer [16]. In this work the synthesis and characterization of Cu(II), Ni(II), and Co(II) complexes with metformin and cysteine as mixed ligands are investigated.The chemical structures of the ligands which were studied as shown in Figure-1.



(MTF)

(Cys)

Figure 1-The structures of the ligands (MTF,Cys).

Experimental

Materials and Measurements

All the chemicals used in this work were pure grade ($CuCl_2.2H_2O$, $NiCl_2.6H_2O$, $CoCl_2.6H_2O$, Cysteine, NaOH, ethanol, acetone, methanol and chloroform) from BDH. Metformin.HCl was obtained from SDI. N, N-Dimethyl formamide, diethyl ether and dimethylsulfoxide were used from Fluka. FTIR spectra were recorded using (KBr and CsI discs) in the infrared spectrophotometers using SHIMADZU FTIR-8400S and SHIMADZU FTIR-21. The electronic spectra of compounds were measured in DMSO by using UV-Visible Spectrophotometer (Cary-Varian El 04103410) in the region (200-800)nm and a UV-Visible Spectrophotometer in the region (200-1100)nm on a SHIMADZU-1650PC. Elemental analysis (C, H, N and S) were performed by the micro analytical unit on Eurovector EA 3000A. The metal contents were determined by using atomic absorption technique by using Varian- AA6200 Flame Atomic Absorption spectrophotometer. The chloride content for complexes was determined by Mohr's method. The melting points were obtained by using Gallenkamp melting point apparatus. The balance magnetic susceptibility model MSB-MK-I was used to measure the magnetic and the molar conductivity values were measured in DMF solution(10^{-3} M) at room temperature by using WTW series Cand 720. ^{1}H and ^{13}C-NMR spectra were performed in DMSO-d^6 as a solvent on Bruker Ultra shield 300 MHz NMR.

Synthesis of Cu(II),Ni(II) and Co(II) mixed ligands complexes

To an aqueous solution(10ml) of (1mmol) of chloride salts [Cu(II),Ni(II) and Co(II)] (0.170g, 0.237g and 0.237g respectively), an aqueous solution(10ml) of metformin.HCl (0.165g, 1mmol) containing NaOH (0.04g, 1mmol) was added. The mixture was stirred and kept in a boiling water bath for 10 minutes. Then an aqueous solution (5ml) of cysteine (0. 121g, 1mmol) was added with stirring, and heating for 1.5 h in a water bath. The pH was adjusted to 7.5～8.0 with NaOH, intense colored precipitate appeared. The mixture was cooled and filtered then washed with water, followed by absolute ethanol, ether after that was dried over silica gel.

Results and Discussion

The elemental analysis (C.H.N.S) and metal content data of the prepared complexes as shown in Table-1.They were exhibited the formation of (1:1:1) (M:MTF:Cys) molar ratio and were found that the calculated values are in a good agreement with the experimental values.

The prepared complexes were found to be insoluble in most common organic solvents such as methanol, ethanol, chloroform and acetone but they were soluble in DMF and DMSO. The molar conductivity of all complexes in DMF are (14-18) $S.mol^{-1}.cm^{-1}$, which were indicated that the complexes are non- electrolytic [17]; these results were confirmed by performing of the chloride content, which proved the unavailability of this ion.

Table 1- Physical properties of the free ligands and their metal complexes.

Compound	**Color**	**Melting point °C**	**Yield %**	**Elemental analysis (%) Found (Calculated)**				**Metal content(%) found (Calculated)**	**Molar conductivity $S.mol^{-1}.cm^{-1}$**
				C%	**H%**	**N%**	**S%**		
MTF.HCl	White	222-226	-	-	-	-	-	-	-
L-Cys	White	240(dec.)	-	-	-	-	-	-	-
Cu(II)-complex	Olive green	268(dec.)	74	24.35 (24.18)	5.83 (5.75)	24.02 (24.18)	9.11 (9.21)	18.45 (18.29)	15.0
Ni(II)-complex	Light orange	285(dec.)	72	24.34 (24.52)	6.19 (6.10)	23.49 (23.30)	8.74 (8.87)	16.17 (16.28)	18.2
Co(II)-complex	Light olive	262(dec.)	56	23.22 (23.30)	5.79 (5.83)	24.62 24.50)(	9.23 (9.33)	17.32 (**17**.19)	14.4

NMR spectra

^1H and ^{13}C -NMR spectra of free L-cysteine, free metformin.HCl were identified with the help of literature data as follow:

^{1}H-NMR spectra

^1H-NMR assignments for free ligands and their mixed ligands complexes in DMSO are shown in Figures-(2-4) and summarized in Table-2.

In free L-cysteine, signals appeared at 2.85 ppm and 3.12 ppm were attributed to CH(α) and CH_2(β) protons respectively[18]while the signal in ^{1}HNMR spectra of all prepared complexes at (2.79-2.81 ppm) due to the coordination with cysteine [18,19] and a large downfield shift (4.6-4.76 ppm) of NH_2 proton as compared to its value 6.1ppm in corresponding amino acid in the zwitterionic form[20,21]; this was suggested that cysteine is bounded with Cu(II),Ni(II) and Co(II) in their complexes through amino group, In the case of free metformin.HCl, the combined signal was observed at 6.69 ppm due to the NH_2 and NH protons[11,22] which was shifted to downfield in the ^1H-NMR spectra of all prepared complexes[23,24]. Another signal assignable to the methyl protons at 3.3 ppm in the metal complexes spectra that was appeared in 2.92ppm in free metformin[11,23]; whereas a signal of ligand which was referred to imine protons was shifted from 7.15 ppm to (9.18-9.30ppm) in the metal complexes spectra, indicating their coordination through N^2 and N^4 atoms[23,24].

Table 2- ^1H-NMR chemical shifts δ(ppm) of free L-cysteine, free metformin.HCl and their mixed ligands complexes.

Compound	**Chemical shift δ(ppm)**					
	CH(α)	**CH_2(β)**	**NH**	**CH_3**	**(=NH)**	**NH+NH_2**
L-Cys	2.85	3.12	6.10	-	-	-
MTF.HCl	-	-	-	2.92	7.15	6.69
Cu(II) complex	-	-	4.78	3.31	9.30	6.55
Ni(II) complex	2.70	-	4.71	3.36	9.25	6.51
Co(II) complex	2.80	-	4.60	3.33	9.18	6.49

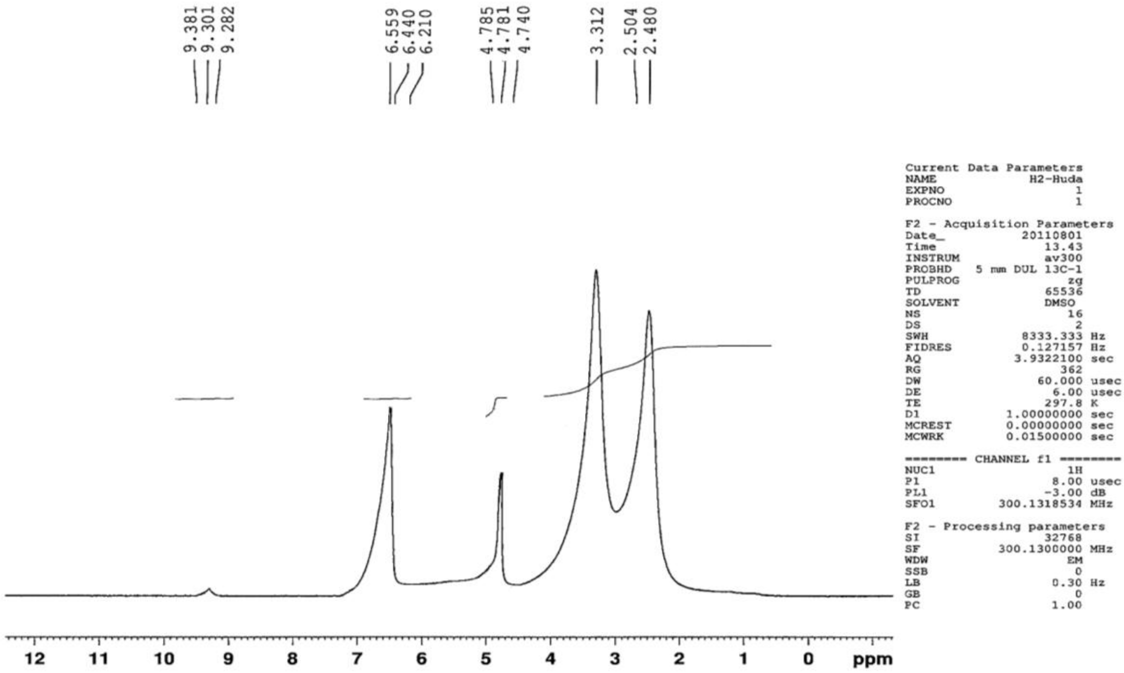


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Figure 2-^{1}H-NMR spectrum of Cu(II) mixed ligands complex.

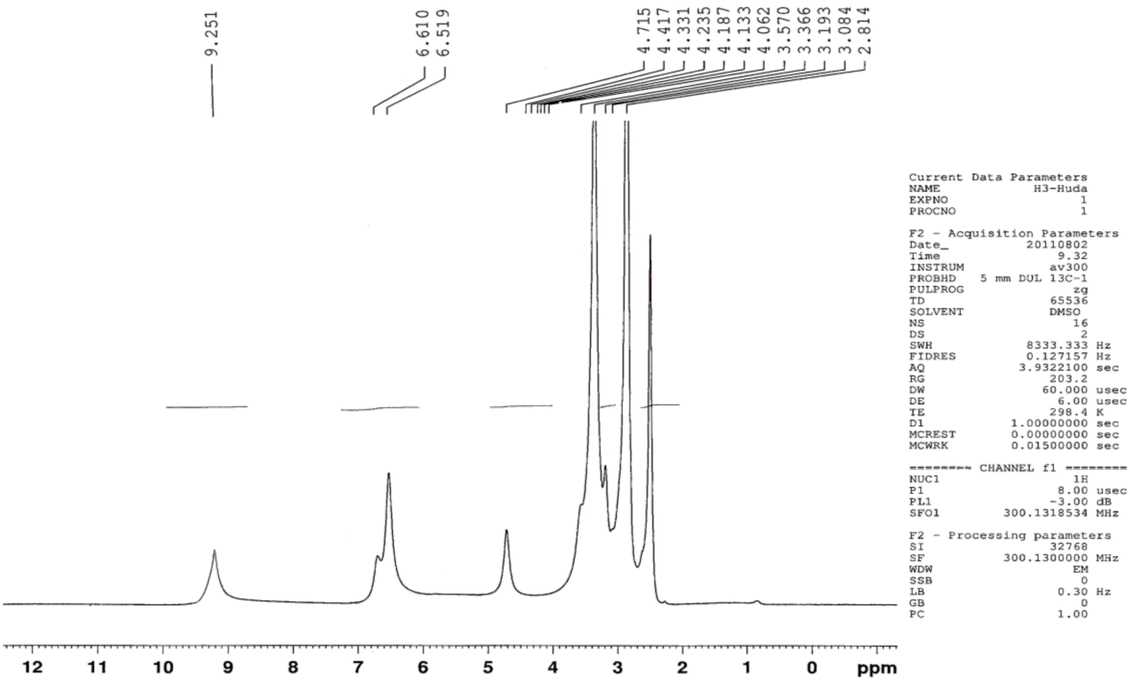

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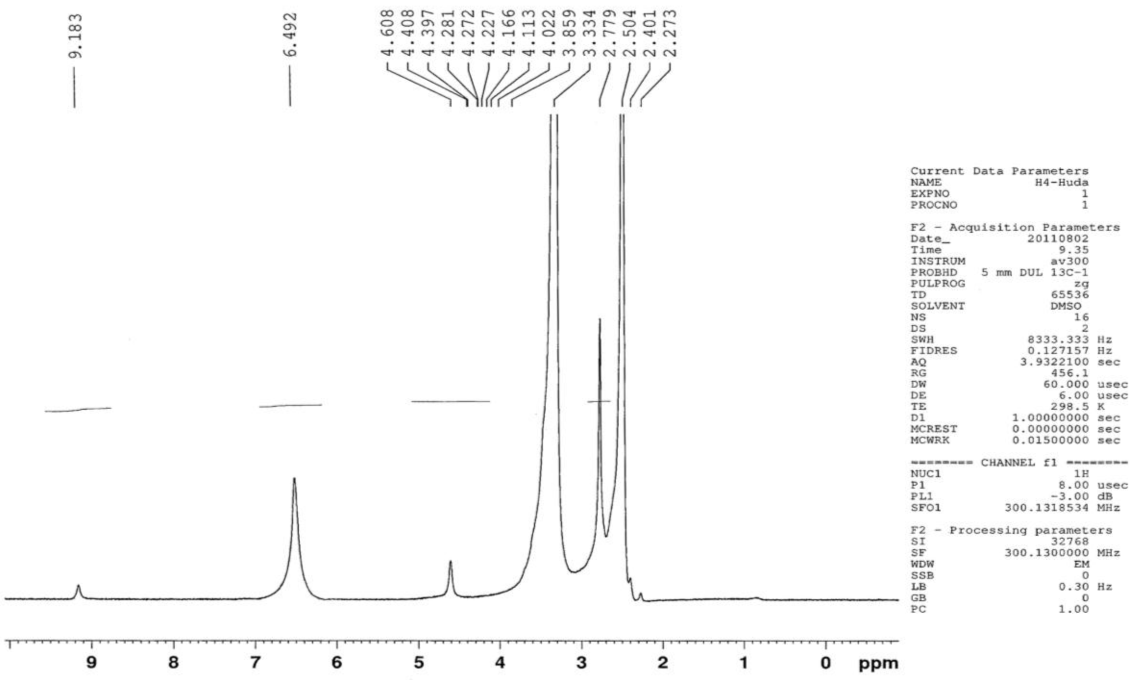
Figure 3-^{1}H-NMR spectrum of Ni(II)mixed ligands complex.



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MCREST         0.00000000 sec
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F2 - Processing parameters
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PC                   1.00
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Figure 4- ^{1}H-NMR spectrum of Co(II)mixed ligands complex.

^{13}C-NMR spectra

In L-cysteine, CH(α) and CH_2(β) resonances were shifted to higher values in the mixed ligands complexes [Table-3, Figures- (5-7)], comparing with these in the free ligand (56.50, 26.12 ppm for CH_2(α) and CH(β) respectively); confirming the involvement of thiol sulphur and amino nitrogen atoms in metal ion coordination [19,25].The signal due to cysteine-COO^- group did not undergo significant chemical shift, because it is not involved in coordinating with the metal ions (Cu(II),Ni(II) and Co(II)) [18].The signals of imine carbon atoms were shifted downfield by (157.18, 157.41 ppm) for all mixed complexes towards the corresponding signals of free metformin.HCl, indicating their participation in chelation[22,23]; while peaks of the primary carbon atoms were observed at (38.49-40.80 ppm) in all mixed complexes spectra, which are assigned at (37.42 ppm) in the free ligand [23].

Table 3- ^{13}C-NMR chemical shifts δ(ppm) of free L-cysteine, free metformin.HCl and their mixed ligands complexes.

Compound	**Chemical shift δ(ppm)**				
	CH(α)	**CH_2(β)**	**COO^-**	**CH_3**	**C=NH**
L-Cys	56.50	26.12	169.86	-	-
MTF.HCl	-	-	-	37.42	158.39 160.06
Cu(II)complex	57.42	30.95	169.52	(39.14-40.80)	157.18 157.21
Ni(II)complex	57.21	31.15	169.41	(38.49-40.80)	157.19 157.41
Co(II)complex	57.37	31.20	169.50	(39.39-40.59)	157.22 157.25

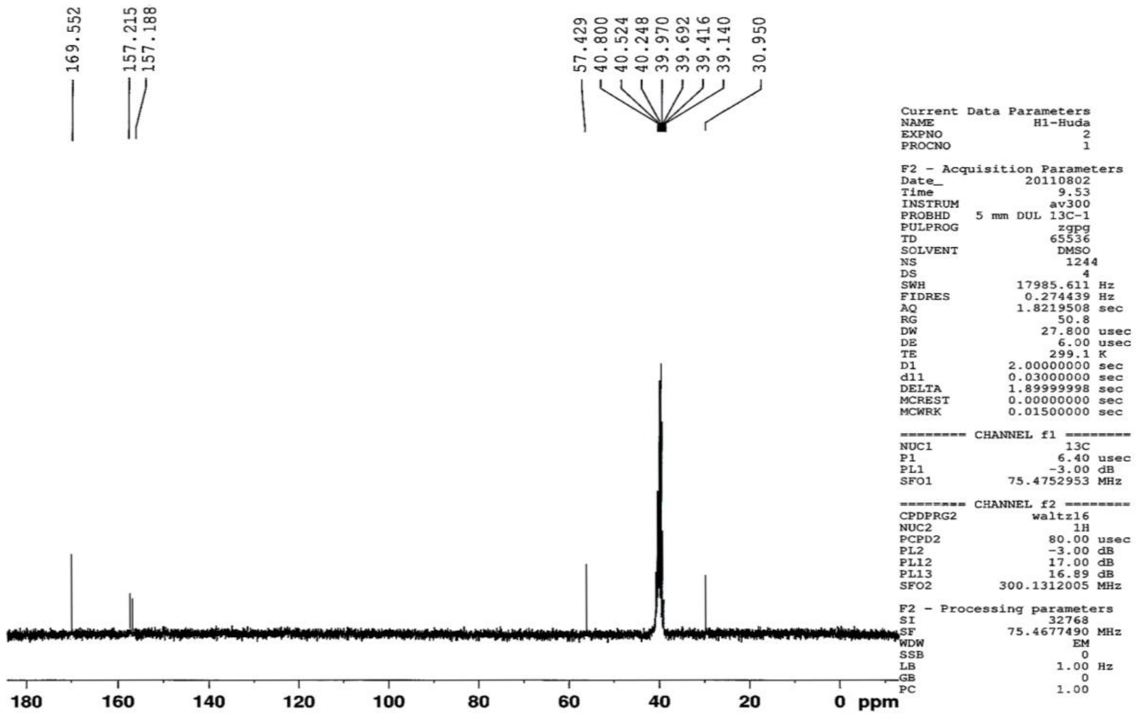

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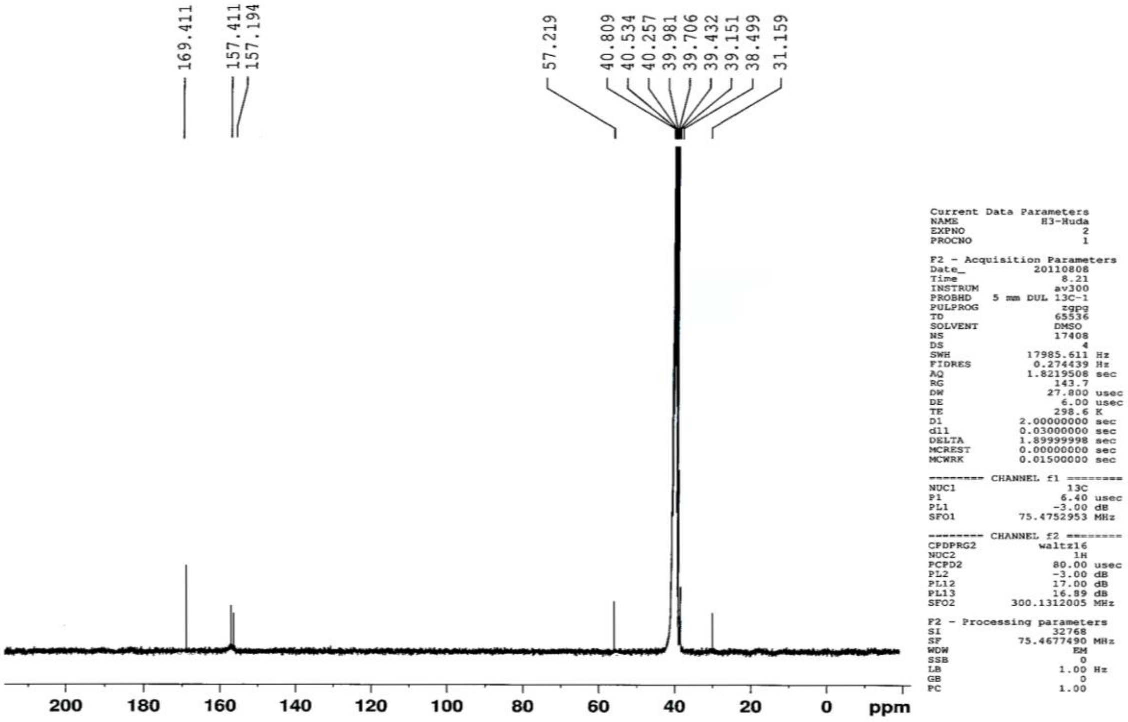
Figure 5- ^{13}C-NMR spectrum of Cu(II) mixed ligands complex.



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P1                    6.40 usec
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SFO1            75.4752953 MHz

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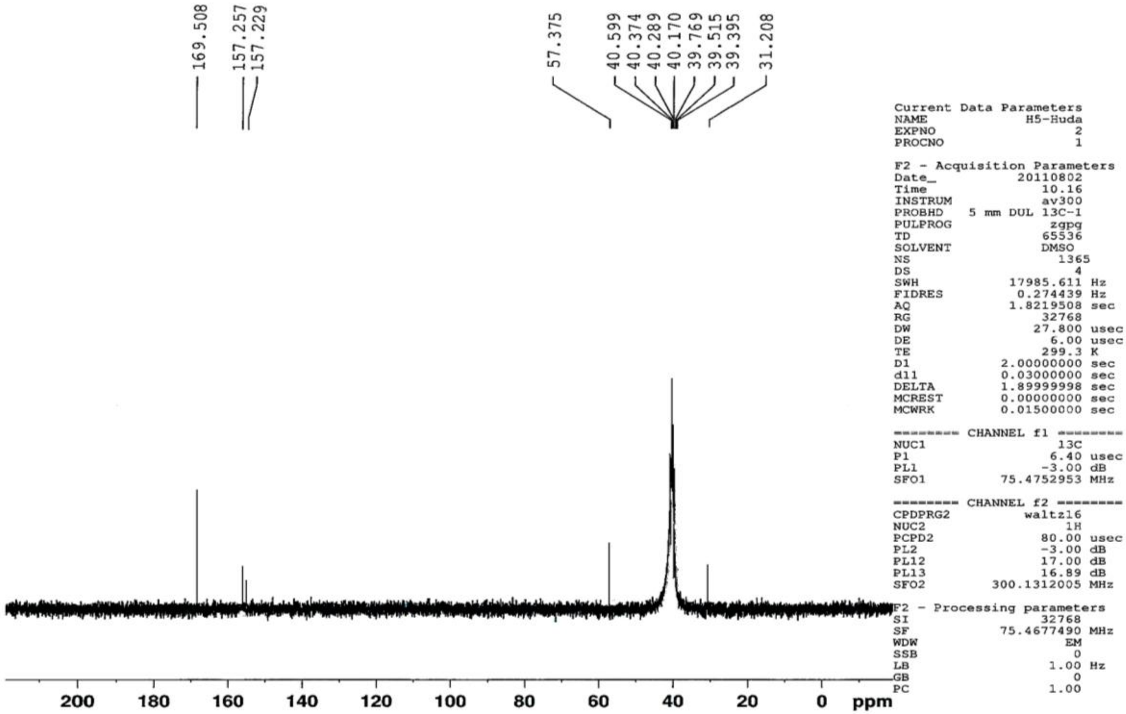
Figure 6- ^{13}C-NMR spectrum of Ni(II) mixed ligands complex.



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SFO1           75.4752953 MHz

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Figure 7- ^{13}C-NMR spectrum of Co(II) mixed ligands complex.

Infrared spectra

The assignments of the frequencies of the vibrational bands (cm^{-1}) of free ligands and all prepared complexes are given in Table-4.

Infrared spectra of free ligands

The infrared spectrum of L-cysteine(zwitterionic form) Figure-8, exhibited significant features, the peaks at 3456 cm^{-1} and 3176 cm^{-1} were assigned to (NH) stretching in protonated amine (NH^{3+}) of L-cysteine[26,27]. The asymmetric and symmetric vibrations (COO^{-}) group were observed at 1589 cm^{-1} and 1392 cm^{-1} respectively, these peaks due to amino twisting, rocking and carboxylate wagging frequencies were observed in the range(1200-600) cm^{-1} [19,25]. An intense absorption band was observed at 2550 cm^{-1}, which was assigned to the (SH) stretching mode [27, 28].

The infrared spectrum of metformin.HCl Figures-9, exhibited an intense absorption bands in the range (3370-3170) cm^{-1} assignable to stretching vibration of (NH) groups [11, 29]. The strong bands were observed at 1627, 1581 cm^{-1} which are due to υ(C=N) and band at 1570 cm^{-1} have been assigned for (NH) deformation [23, 30].

Infrared spectra of prepared complexes with Cu(II),Ni(II)and Co(II).

As regards the chelation of L-cysteine, the new bands were observed at 3210 cm^{-1}, 3209 cm^{-1} and 3207 cm^{-1} due to stretching vibration of (NH) in the prepared complexes of Cu(II),Ni(II)(Figure-10) and Co(II) respectively[19,27], indicates that the coordination through the nitrogen of amino group. No shift was observed in the asymmetric and symmetric stretching vibration of (COO^{-}) group of L-cysteine, this supports the non-involved of cysteine-(COO^{-}) group in the coordination with metal [19]. The corresponding vibration υ(C-S) in all mixed ligands complexes was shifted to lower frequencies indicated that L-cysteine coordinated with metal ions through the sulfur atom [18].

Whereas in the case of metformin.HCl ligand, the new strong bands in the range (1685-1650 cm^{-1}) are assigned to the coordinated imino groups[30, 31]. The formation of a chelate ring is supported by the appearance of a new band at (1365-1200 cm^{-1}) assigned to ring vibration [11, 23]. The low intensity bands were observed in the range (435-420 cm^{-1}), which are assigned to υ(M-N) stretching [11,32].

Table 4- Characteristic IR stretching vibrations (cm-1) of the free ligands and their complexes

	Groups (cm^{-1})	**Compounds**				
		L-Cys	**MTF**	**Cu(II)-complex**	**Ni(II)-complex**	**Co(II)-complex**
L-Cys	υ(N-H)	3456 3176	-	3210	3209	3207
	$\upsilon_{asy}(COO^-)$	1589	-	1616	1610	1610
	$\upsilon_{sy}(COO^-)$	1392	-	1396	1409	1398
	υ(C-S)	694	-	400	385	375
	υ(M-N)	-	-	475	478	445
	υ(M-S)	-	-	675	665	676
	υ(S-H)	2550	-	-	-	-
MTF.HCl	$\upsilon_{asy}(NH_2)$	-	3371	3463	3429	3460
	$\upsilon_{sy}(NH_2)$	-	3170	3266	3271	3238
	υ(NH)	-	3321 3294	3392 3348	3371 3344	3377 3346
	υ(M-N)	-	-	435	438	430
	υ(C=N)	-	1627	1685	1685 1652	1679
	$\upsilon_{chlate\ ring}$	-	-	1365	1299	1296
H_2O lattice (coordinate)		-	-	(3550,705,914)	3350 (3483,702,891)	(3525,723,887)

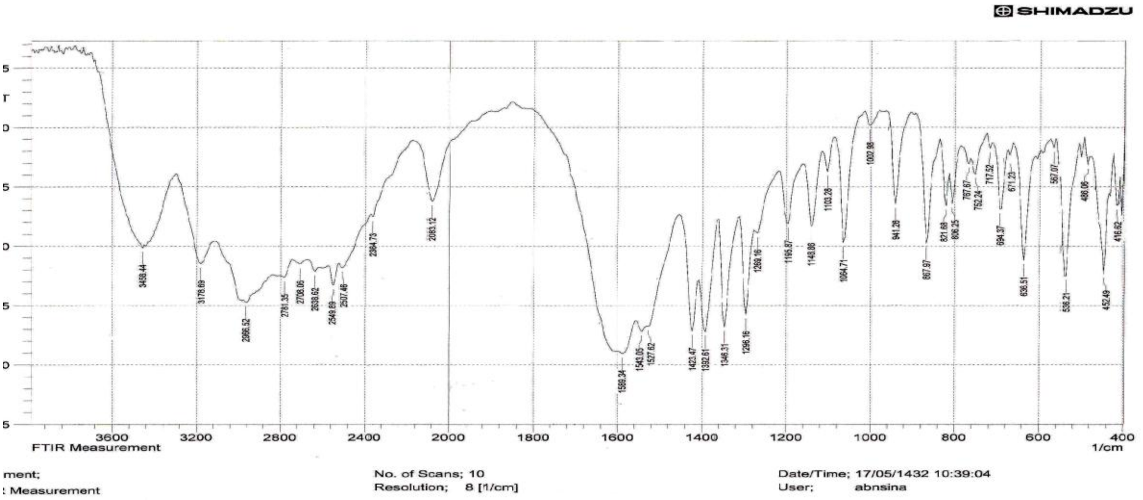


Figure 8- FT-IR spectrum of L-Cysteine.

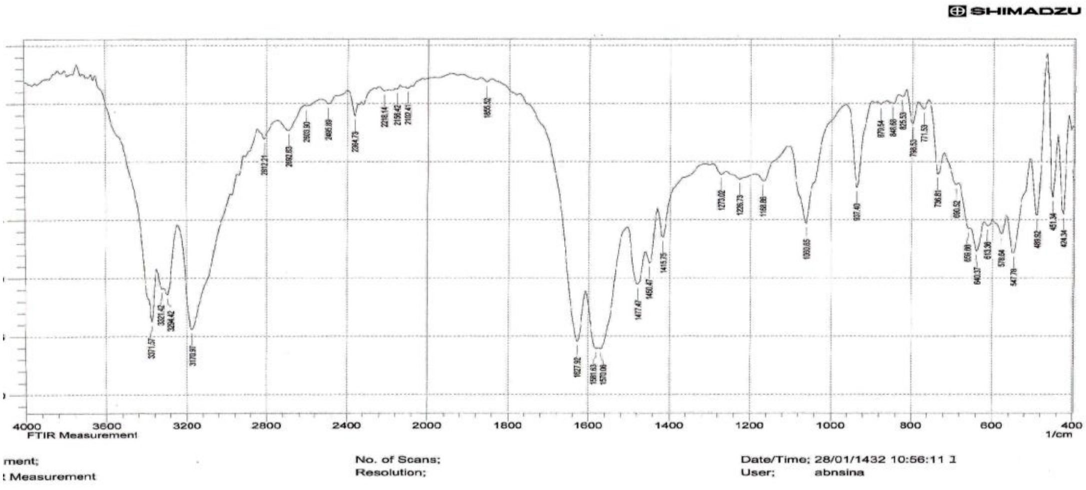


Figure 9- FT-IR spectrum of Metformin.HCl

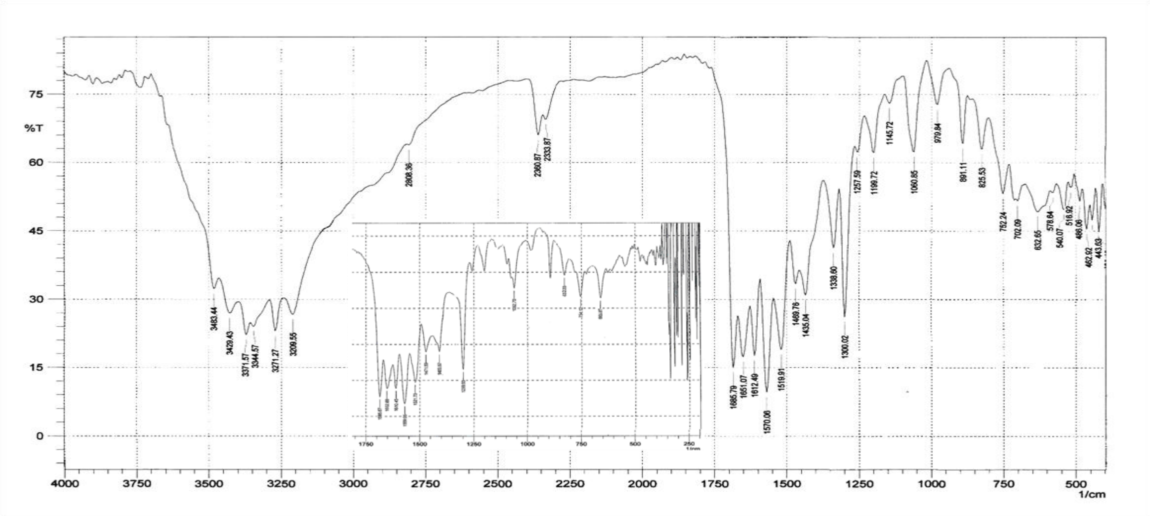


Figure 10- FT-IR spectrum of Ni(II) mixed ligand complex.

Magnetic susceptibility measurements

The magnetic moment value (μeff) of Cu(II)-complex (d^9) is 1.85B.M , this value refers to a distorted octahedral Cu(II)-complex[33]. The magnetic moment of Ni(II)-complex (d^8) was found to be 3.10B.M, which is in fair agreement with the predicted value of octahedral geometry[34]. Whereas Co(II)-complex (d^7) has μ_{eff} =4.9 B.M, which indicates that it is of high spin octahedral type [35].

The electronic spectra

The electronic spectra of free ligands and their complexes are given in Table-5. Electronic spectrum of Cys in DMSO, Figure-11 showed an absorption band at 277nm (36101 cm^{-1}), which can be attributed to ($\pi\rightarrow\pi^*$) transition [36]. Electronic spectrum of MTF.HCl in DMSO, Figure-12 showed an absorption band at 255 nm (39215 cm^{-1}), which can be attributed to ($\pi\rightarrow\pi^*$) transition of (C=N) in the biguanide group [37].

The spectrum of Cu(II) complex Figure-13, displayed a band at 669nm(14947 cm^{-1}) that can be assigned to $^2Eg\rightarrow^2T_2g$ transition, indicating the Cu(II) complex has distorted octahedral geometry[38,39]. Electronic spectrum of Ni(II) complex ,showed three bands at 1025nm(9756cm^{-1}),711nm (14064cm^{-1}) and 444nm(22522 cm^{-1}).

These were assigned to the transitions $^3A_2g\rightarrow^3T_2g(F)(\nu_1)$, $^3A_2g\rightarrow^3T_1g$ $(F)(\nu_2)$ and $^3A_2g\rightarrow^3T_1g(P)(\nu_3)$ respectively of octahedral geometry[40] and the band at 914nm (10940 cm^{-1}) was attributed to the forbidden transition $^3A_2g\rightarrow^1Eg$ [41]. We can be calculated the values of 10Dq, B' and Dq/B' from ν_3/ν_2 (1.60) ratio and using (Tanabe-Sugano) diagram for d^8, the value of β(0.634) indicated a covalent character [42].The electronic spectrum of the Co(II) complex, exhibited three bands at 1015 nm (9852 cm^{-1}), 718nm (13927 cm^{-1}) and 498nm (20080 cm^{-1}) that can be assigned to the transitions $^4T_1g\rightarrow^4T_2g(F)(\nu_1)$, $^4T_1g\rightarrow^4A_2g(F)(\nu_2)$ and $^4T_1g\rightarrow^4T_1g(P)(\nu_3)$ respectively, suggesting an octahedral geometry around Co(II) ion[41]. By using (Tanabe-Sugano) diagram for d^7 and from ν_3/ν_1 (2.03) ratio, we can be calculated the values of 10Dq, B' and Dq/B', the value of β(0.760) indicates that the complex has covalent character [41]. Figure-14 shows the proposed structure for all prepared complexes.

Table 5- The data of electronic spectra and ligand field parameters of their complexes.

Complex	Absorption bands (cm^{-1})	Transition character	B	10Dq	B'	Dq/ B'	β
Cu(II) complex	14947	$^2Eg\rightarrow{}^2T_2g$	-	-	-	-	-
Ni(II) complex	9756 ν_1 14064 ν_2 22522 ν_3	$^3A_2g\rightarrow{}^3T_2g$ (F) $^3A_2g\rightarrow{}^3T_1g$ (F) $^3A_2g\rightarrow{}^3T_1g$ (P)	1030	9414	653.7	1.44	0.634
Co(II) complex	9852 ν_1 13927 ν_2 20080 ν_3	$^4T_1g\rightarrow{}^4T_2g$ (F) $^4T_1g\rightarrow{}^4A_2g$ (F) $^4T_1g\rightarrow{}^4T_1g$ (P)	971	6127	752	0.83	0.760

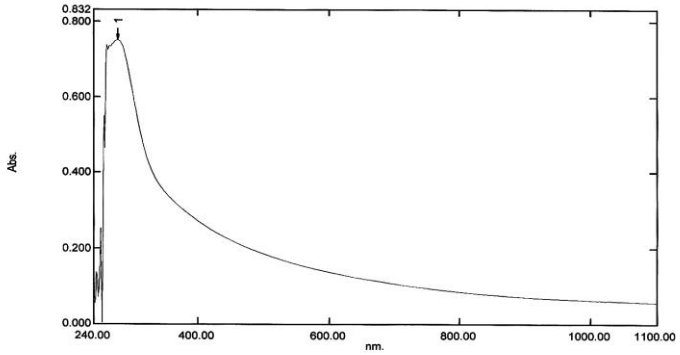


Figure 11-Electronic spectrum of Cysteine in DMSO.

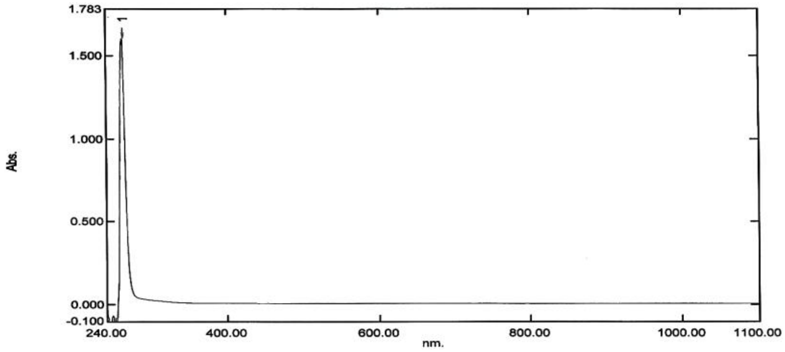


Figure 12- Electronic spectrum of Metformin.HCl in DMSO.

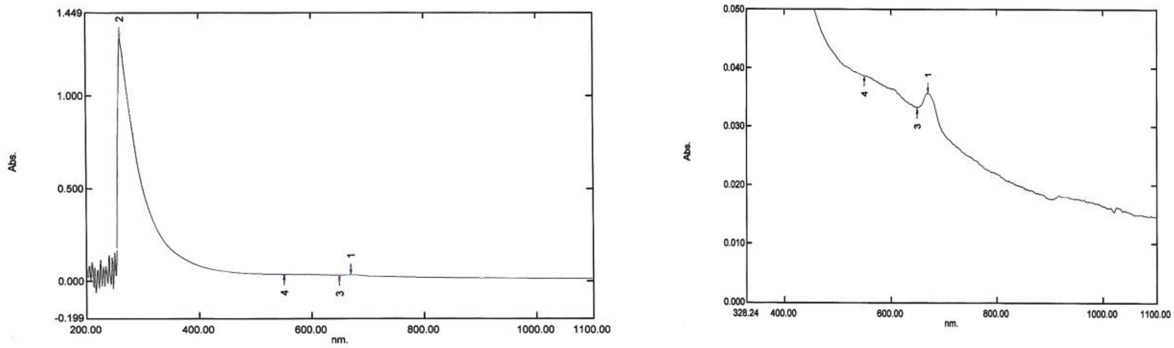
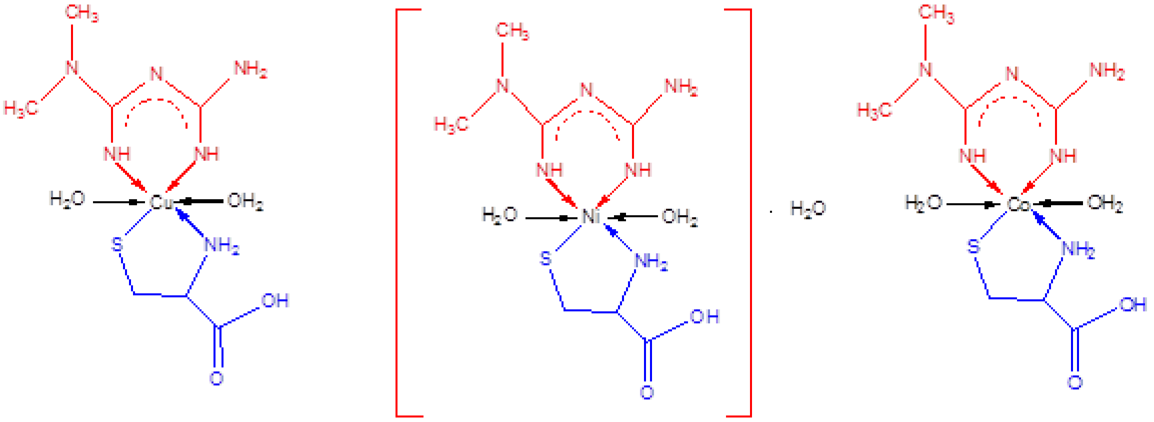


Figure 13- Electronic spectrum of Cu(II) mixed ligand complex in DMSO



[Cu(MTF)(Cys)(H_2O)$_2$] **[Ni(MTF)(Cys)(H_2O)$_2$].H_2O** **[Co(MTF)(Cys)(H_2O)$_2$]**

Figure 14-The Proposed structure for all prepared complexes.

Conclusions

In this study, new mixed ligand complexes of Cu(II), Ni(II) and Co(II) derived from metformin(MTF) as primary ligand and cysteine (Cys) as second ligand have been synthesized. The molar conductivity of the complexes measured in DMF solution showed that the complexes were non-electrolytic. The spectroscopic Studies of all mixed ligands complexes indicate that cysteine is coordinated with metal ion through sulphur atom and nitrogen of amino group, while metformin acts as a bidentate ligand, coordinated to metal ions through the nitrogen N^2 and N^4 atoms. Thus, from the results presented the metal complexes have an octahedral geometry, as shown in Figure-8.

References

1. Budavari, S. **2001**. *The Merck Index*. Thirteenth Edition, Merck & Co. Inc.
2. Krentz, A.J. and Bailey, C.J. **2005**. Oral Antidiabetic Agents. *Drugs*, 65(3), pp: 385-411.
3. Dornan,T.Heller,S.Peck,G. and Tattersal,R.**1991**. Double-blind evaluation of efficacy and tolerability of metformin in NIDDM.*Diabetes care*, 14(4),pp: 342-344.
4. Siest,G.Roos,F. and Gabou,J.J. **1963**.Dosage du NN dimethylbiguanidepar le diacetyleen milieu alcaline. *Bull. Soc. Pharm. Nancy*, 58, pp: 29-38.
5. Pignard,P. **1962**. Spectrophotometric determination of N,N-dimethylbiguanide in blood and urine . *Ann.Biol.Clin*, 20, pp: 325-330.
6. Woo,L.C., Yuen,V.G. and Thompson,K.H.**1999**. Vanadyl–biguanide complexes as potential synergistic insulin mimics. *J. Inorg. Biochem*., 76(3-4), pp:251-257.
7. Bentefrilt,F. Morgent,G. Viossat,B. Leonce,S. Gui lbaud,N.Pierre,A.Atassi,G. and Huy,N.**1997**. Synthesis and antitumor activity of the metformin platinum (IV) complex. Crystal structure of the tetrachloro(metformin)platinum (IV)dimethylsulfoxide solvate.*J.Inorg.Biochem*.,68(1), pp:53-59.
8. Lemoine,P.Chiadmi,M.Bissery,V.Tomas,A. and Viossat,B.**1996**. Les Composés de la Metformine avec les Ions Co^{II}, Cu^{II} et Ni^{II}.*Acta. Cryst*., C52, pp:1430-1432.
9. Zhu,M. Lu,L.Jin,X. and Yang,P.**2002**.Trichloro(1,1-dimethylbiguanidium-N^3)zinc(II). *Acta. Cryst*., C58, pp:m158-m159.
10. Viossat,B.Tomas,A. and Dung,N.H.**1995**.L'hydrogénocarbonate de Bis(N,N-diméthylbiguanide) Cuivre(II), [Cu(C4H11N5)2]2HCO3, Acta.Cryst., C51, pp:213-215.
11. Olar,R. Badea,M.Cristurean,E.Lazar,V.Cernat,R. and Ballotescu,C.**2005**.Thermal behavior, spectroscopic and biological characterization of Co(II), Zn(II), Pd(II) and Pt(II) complexes with N,N-dimethylbiguanide. *J.Therm.Anal.Calorim*., 80, pp:451-455.
12. Allain,A. Kubiak,M. Jezowska-Trzebaitowska,B. Kozlowdki,H. and Glowaik,T. **1980.** NMR and x-ray studies of Pd(II) and Pt(II) complexes with S-methyl-L-cysteine sulfoxide.*Inorg. Chim. Acta*., 46, pp: 127-132.
13. Domazetis,G. Mackay,M.F. Magee,R.J. and James,B.D. **1979.** Interaction of organotin compounds with biological ligands and the molecular structure of -ethyl L- cysteinato S,N(chlorodimethyl)stannate(IV) *Inorg. Chim. Acta*, 34, pp: L247-L248.
14. Lenz, G.R. and Martell,A.E. **1964**. Metal chelates of some sulfur-containing amino acids. *Biochem*., 3(6), pp:745-750.
15. Masoud,M.S. and Abd El. Hamid,O.H.**1989**. Structural chemistry of amino acid complexes. *Trans. Metal. Chem*., 14(3), pp: 233-234.
16. Goodman, A. Goodman, S. Rall, W. and Murad, F. **1985**.*The pharmacological Basis of Therapeutics*, Seventh Edition, Macmillan, New York.
17. Geary,J.T.**1971**. The use of conductivity measurements in organic solvents for the characterisation of coordination compounds. *Coord.Chem.Rev*., 7(1),pp:81-122.
18. Chasapis,C.T.Hadjikakou,S.K.Garoufis,A. and Ming,Y.**2004**. Organotin(IV) Derivatives of L-Cysteine and their in vitro anti-tumor properties. *Bioinorganic Chemistry and Application*,2(1-2),pp:43-53.
19. Redy,P.R. Radhika,M. and Manjula,P.**2005**.Synthesis and characterization of mixed ligand complexes of Zn(II) and Co(II) with amino acids: relevance to zinc binding sites in zinc fingers, *J. Chem. Sci*., 117(3),pp:239-246.

20. Mital,R.Srivastava,T.S. Parekh,H.K. and Chitnis,M.P.**1991**. Synthesis, characterization, DNA binding, and cytotoxic studies of some mixed-ligand palladium(II) and platinum(II) complexes of α-diimine and amino acids. *J. Inorg. Biochem*, 41(2), pp:93-103.

21. Kumar,L. Kandasamy,N.R. Srivastava,T.S. Amonkar,A.J.Adwankar,M.K.and Chitms,M.P.**1985**. Synthesis and spectroscopic studies of potential anticancer [platinum(II)(2,2' -bipyridine)(amino acid)]$^{n+}$ (n = 1 or 2) complexes, *J. Inorg. Biochem*., 23(1),pp:1-11.

22. Gadape,H.H. and Parikh,K.S.**2011**. Quantitative determination and validation of metformin hydrochloride in pharmaceutical using quantitative nuclear magnetic resonance spectroscopy , *E-Journal of Chemistry* ,8(2),pp:767-781.

23. Olar,R. Badea,M. Marinescu,D. ChiFiriuc,M. Bleotu. **2010**. *N,N*-dimethylbiguanide complexes displaying low cytotoxicity as potential large spectrum antimicrobial agents, *Eur, J. Med. Chem*., 45(7), pp:3027-3034.

24. Marchi,A.Marvelli,L. Neves,M. and Feeretti,V.**1999**. Technetium(V) and rhenium(V) complexes of biguanide derivatives. crystal structures, *J.Chem.Soc.,Dalton Trans*.,(12),pp:1937-1943.

25. Ahmed,I.T. **2007**. Spectroscopic, thermal and electrochemical characterization of synthesized divalent transition metal complexes with cysteine and 4-substituted thiosemicarbazides, *Trans. Metal. Chem*., 32(5), pp: 674-678.

26. Kieninger,M. and Ventura,O.N.**2010**. On the structure, infrared and Raman spectra of the 2:1 cysteine–Zn complex, *Theor.Chem.Acc*, 125(3-6), pp: 283-287.

27. Susi,H. Byler,D.M.Gerasimowicz,W.V.**1983**. Vibrational analysis of amino acids: cysteine, serine, β-chloroalanine, *J.Molecular Structure*, 102(1-2), pp: 63-79.

28. Domazetis,G.Magee,R.J. and James,B.D. **1978**. Organotin (IV) derivatives of L-cysteine and DL-penicillamine, *J. Organomet. Chem*., 162(2), pp: 239-252.

29. Patrinoiu,G.Patron,L.Carp,O and Stanica,N.**2003**.Thermal behaviour of some Iron(III) complexes with active therapeutically biguanides, *J.Therm. Anal.Calorim*., 72(2), pp:489-495.

30. Babykutty,P.V.Prabhakaran,C.P.Anautaraman,R. and Nair,C.G.R.**1974**.Electronic and infrared spectra of biguanide complexes of the 3*d*-transition metals, *J. Inorg. Nucl. Chem*, 36(12), pp: 3685-3688.

31. Olar,R. Badea,M and Marinescu,D.**2010**. Thermal study of some new Ni(II) and Cu(II) complexes with ligands derived from N,N-dimethylbiguanide as potential antimicrobials, *J.Therm.Anal.Calorim*., 99(3), pp:893-898.

32. Olar, R. Badea, M. Marine scn, D. Lazar, V. Balotescu, C. and Cristurean, E. **2007**. Thermal behavior of some N, N-dimethylbiguanide derivatives displaying antimicrobial activity, *J.Therm. Anal. Calorim*., 88(2), pp:323-327.

33. Dubey,K.P.K achru,C.N. and Wazri,B.L.**1979**. Metal chelate complexes of the schiff bases derived from salicylaldehyde and methyl ethers of aminophenols (Anisidines).*J.Chinese Chem. Soc*,26(1),pp:37-41.

34. Patra,A.K. Netaji,M. and Chakravarthi,A.R.**2007**. Synthesis, crystal structure, DNA binding and photo-induced DNA cleavage activity of (S-methyl-l-cysteine)copper(II) complexes of heterocyclic bases, *J.Inorg.Biochem*.,101(2),pp:233-244.

35. Arora,O.P. Sankhla,D.S. and Sudhindra,M.N. **1989**. Mixed ligand complexes of bis(Salicylaldehydato) copper(II) with thioyrea and substituted thioureas. *Indian Natn.Sci.Acad*., 46(4),pp:378-380.

36. Bancu,L. Carp,O. and Jitaru,I. **2006**.Ni(II) ternary complexes containingdiimineand cycteine, *Revue Roumaine de Chimie*, 51(6),pp:497-502.

37. Nandi,S.D. **1972**. Spectrophotometric(UV)investigation on biguanide and substituted biguanides. *Tetrahedron*,28, pp:845–853.

38. Sangeetha,N.R. Baradi,K. Gupta,R.Pal,C.K.Manivannan,V. and Pal,S.**1999**. Synthesis, structure and properties of a dicopper(II) complex, *Polyhedron* ,18(10),pp:1425-1429.

39. Karunakaran,S. and Kandaswamy,M.**1995**. Synthesis, electrochemical and magnetic properties of new acyclic 'side-off' binuclear copper(II) complexes, *J.Chem.Soc., Dalton Trans*.,(11), pp:1851-1855.

40. Zhu,D.R. Song,Y. Xu,Y. Zhang,Y. Raj,S.S.S. Fun,H.K. and You,X.Z.**2000**. Syntheses, crystal structures and properties of the novel Co(II) and Ni(II) complexes with 4-(*p*-methylphenyl)-3,5-bis(pyridin-2-yl)-1,2,4-triazole,*Polyhedron*, 19(18-19),pp:2019-2025.

41. Lever,A.B.P. **1968**. *Inorganic electronic spectroscopy*, First Edition, Elesvier Publishing Company Amsterdum-London-New York.
42. Lever, A.B.P.**1968**.Electronic spectra of some transition metal complexes: Derivation of Dq and B, *J.Chem.Edn*.,45(11),pp:711.