RESEARCH ARTICLE

Synthesis, Characterization, and Biological Studies of New Complexes Derived from 2-(1H-Benzimidazol-2-yl) Aniline

Bahaa A. Al-Hadi,[1] Eman A. Othman,[2] Lekaa K. A. Karem[1*]

[1]*Department of Chemistry. College of Education, University of Samarra, Baghdad, Iraq*
[2]*Chemistry Department, College of Education for Pure Sciences Ibn Al-Haitham, University of Baghdad, Baghdad, Iraq*

Received: 30th July, 2021; Revised: 17th August, 2021; Accepted: 27th August, 2021; Available Online: 25th September, 2021

ABSTRACT

The Schiff base (E)-2-(((2-(1H-benzo[d]imidazol-2-yl) phenyl) imino) methyl)-4-methylphenol (Lb) ligand with some metals(II) ion such as; Co, Cu, Cd, and Hg, were synthesis and characterized by the mass and ^{1}HNMR spectrometry for ligand Schiff base, the fourier-transform infrared spectroscop (FTIR), UV- visible and the flame atomic absorption (AA) spectrum, the CHN analysis, and the chlorine content, in addition to measuring the magnetic sensitivity of the complexes. All the complexes had octahedral geometry. The bioactivity activity for compounds against; *Rhizopodium, Staphylococcus aureus,* and *Escherichia coli* showed different efficacy towards these microorganisms.

Keywords: Ligand Schiff Base, Microorganisms, Schiff Base, Spectrometry.

International Journal of Drug Delivery Technology (2021); DOI: 10.25258/ijddt.11.3.48

How to cite this article: Al Hadi BA, Othman EA, Karem LKA. Synthesis, Characterization, and Biological Studies of New Complexes Derived from 2-(1H-Benzimidazol-2-yl) Aniline. International Journal of Drug Delivery Technology. 2021;11(3):937-941.

Source of support: Nil.

Conflict of interest: None

INTRODUCTION

Benzimidazole is a fraction containing a benzene ring and an imidazole heterocyclic ring. A benzimidazole derivative is an essential class of biologically active molecules in the field of drugs and pharmaceuticals.[1] The substituting analogs of benzimidazole have a wide range of bioactive compounds, anti-inflammatory,[2,3] anti-fungal and anti-bacterial activity,[4] antiviral,[5] anti-hypertensive,[6] human glucagon receptor antagonist and infection control activities.[7] The synthesis, characterization, and anti-proliferative activity of a novel Schiff base based on benzimidazole (HL) and [(Cu(L)NO_3)$_2$] complex are described. Various physicochemical techniques investigated the DNA-protein binding studies.[8] A new bi-benzimidazole synthesis of the Schiff base ligand has been described, ^{13}C NMR, ESI-MS, UV-vis, and fluorescence) and X-ray single-crystal analyzes. The excellent selectivity of H3L towards Cu(II) and Al(III) was determined via distinct responses under mixed aqueous conditions by spectroscopic studies. [9] Conventional and microwave irradiation methods synthesized a new class of Schiff bases bearing benzimidazole moiety. With an emphasis on speed, increasing reaction rates, and yield of products, the microwave irradiation method is reliable. Furthermore, CoII, CuII, NiII and ZnII complexes of Schiff base[13] were synthesized and examined for their anticancer activities in-vitro and in-vivo.[10] Novel complex derived from 2-aminomethyl-benzimidazole, 2-(1H-benzimidazol-2-yl) aniline, and metal chloride (Cd (II), Ni(II), and Cu(II)) was successfully synthesized.[11] In this research, new complexes of cobalt (II), copper (II), cadmium (II), and mercury (II) ions were prepared, diagnosed, and biological activity study with a Schiff base ligand as Tri-dentate. All complexes have octahedral structures.

EXPERIMENTAL AND METHODS

Chemicals used in the laboratory are of the highest purity that does not need any further purity, and they have been purchased from distinguished sources. The device used to measure the melting point is Stuart Melting Point Kit, the CHN for all compounds is measured by Euro (EA 3000), ultra Violet-Visible spectra are performed on a Shimadzu UV-160A. In KBr discs, the NMR and mass spectra were performed on by "Brucker DRX system 500 (500 MHz)" and Shimadzu, E170Ev., the FTIR spectra are verified via FTIR-8400S Spectrophotometer on 4000–200 cm^{-1}, atomic absorption method utilizing AA 620G Shimadzu spectrophotometer; magnetic sensitivity was measured using a Faraday's method using Bruker BM6 instrument. The complexes and their metal substances have been examined via Shimadzu AA (620 G) atomic absorption spectrophotometer.

Synthesis of Ligand

A solution of 2-(1H-Benzimidazol-2-yl) aniline [12] (1 mmol, 0.209 g in 10 mL ethanol has been inserted to a mixture solution of in 10 mL ethanol 2-hydroxy-5-methyl-benzaldehyde (0.136 g, 1 mol) and 2–3 drops of glacial acetic acid, the product

*Author for Correspondence:dr.likaakhalid@gmail.com

combination has been refluxed for 4 hours. The resulted orange solid is composed of filtration, recrystallization from acetone absolute, and dried.

Synthesis of Complexes

A solution 1-mmol of ligand Schiff base in 10 mL absolute ethanol was added with stirred to a solution consisting of 1 mmol and 10 mL ethanol and Co(II) chlorid. $6H_2O$, Cu(II) chlorid. $2H_2O$, Cd (II) chlorid. H_2O, and Hg (II) chloride). The product mixture is stirred for sixty minutes and, then the result is filtered and dried through anhydrous $CaCl_2$.

Biological Activity

The prepared compounds were tested against *Escherichia coli*, *Staphylococcus aureus,* and *Rhizopodium* by disc diffusion technique. The sample solution is prepared from the concentration of 0.001 M in DMSO as a solvent. The dishes are incubated for 24 hours at room temperature then the diameter of the inhibition is measured, which indicates the growth of bacteria.

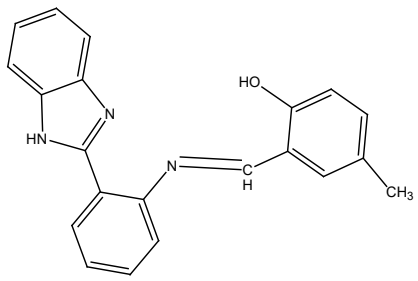
RESULT AND DISCUSSION

The solubility test results showed in DMF and DMSO and insoluble in H_2O, conductivity values of all complexes were 3-18 Ω^{-1} cm^2 mol^{-1}. The CH N analysis and the atomic absorption of the complexes (1–4) are listed in Table 1. The suggested formula for the complexes is $[M(L)(Lb)_2]$ when M (II) ions = Co, Cu, Cd, and Hg.[13]

Mass Spectrum

Mass spectrum of the ligand L was recorded Figure 1. The spectrum showed a group of different fission peaks with M. wt with the difference in their multitude through the peak fractionation at M^+=326.2 (m/e) attributed to the partial ion of the ligand $C_{21}H_{17}N_3O$.[14,15]

2-(1H-Benzimidazol-2-yl)aniline 2-hydroxy-5-methylbenzaldehyde



(*E*)-2-(((2-(1*H*-benzo[*d*]imidazol-2-yl)phenyl)imino)methyl)-4-methylphenol

Equation 1: The preparation of ligand schiff base

NMR Spectrum

The ^{1}HNMR spectrum of the ligand (Figure 2) was prepared using the solvent DMSO and (TMS) as a basic reference, as shown in Table 2 and Figure 3. Where the spectrum showed the signal appeared at (1.12, 1.10) ppm, which refers to the protons of the -CH_3 group associated with the two benzene rings, while the signal in (2.51–2.49) ppm) refers to DMSO solvent, a signal at (3.4, 3.77) ppm where it indicates the presence of H_2O in the ligand, while the single signal at the site (10.21 ppm) it refers to the proton of the phenolic (OH) group. Also, multiple signals that appeared in the region (7.58–6.89) ppm were attributed to the aromatic ring's protons, while the single signal in the 8.83 ppm is attributed to the proton of -CH=N group.[16]

FTIR Spectral

The infrared spectra of 1, 2, 3, and 4 complexes Table (3–4) showed absorption bands within the range (1666–1652) cm^{-1},

Type of fragment	*Mass/Change (m/z)*
M+	326
$[M-C_5H_4]+$	262
$[M-CH_4N_2]+$	221
$[M-C_5H_3]+$	158
$[M-C_2H]+$	96
[M-CHO]+	67
$[M-CH_3]+$	52

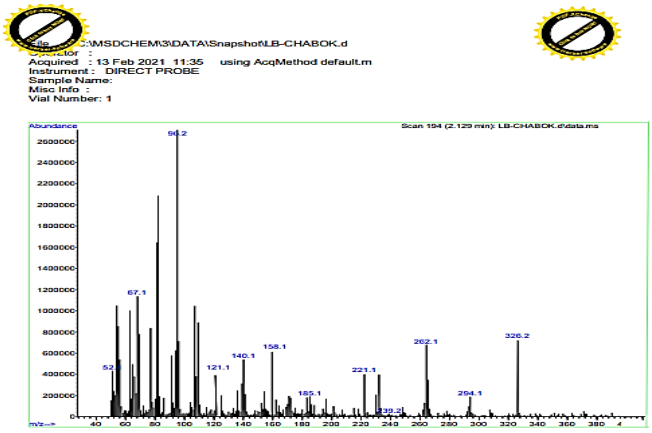


Figure 1: Mass Spectrum of L

Table 1: Physical properties and conductivity of prepared compounds.

Compounds	*M.wt g/mole*	*M.P °C*	*Color*	*Elemental analysis*				*Cond. Ω^{-1}*
				C	*H*	*N*	*M*	
C21H17N3O	327.29	172-170	Yellow	77.00 77.04	5.11 5.23	12.63 12.84	—	—
$[Co(Lb)_2]$	712	210-212	Orange	70.88	4.53	11.81	8.28	14
$[Cu(Lb)_2]$	716	123-135	Pail - brown	70.43	4.50	11.73	8.87	18
$[Cd(Lb)_2]$	765	140-145	Brown	65.93	4.22	10.98	14.69	5
$[Hg(Lb)_2]$	853	281 des	Pail-brown	59.12	3.78	9.85	23.51	3

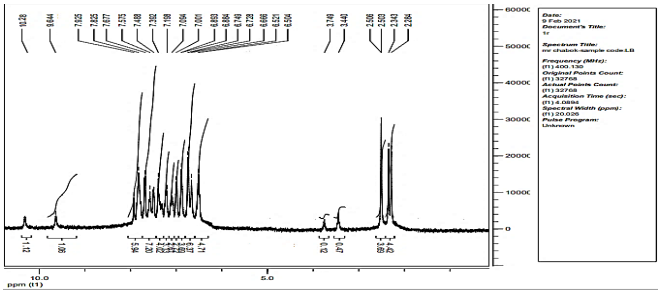


Figure 2: The NMR for ligand L

Table 2: The FTIR spectra bands of compounds.

Comp.	*υ (C=N) Schiff*	*υ (C=N)*	*C=C)) υ ring*	*M-N*	*M-O*
LB	1672	1622	1583	—	—
$[Co(Lb)_2]$	1653	1618	1591	669 646	455
$[Cu(Lb)_2]$	1658	1600	1554	671 622	459
$[Cd(Lb)_2]$	1652	1620	1558	669 640	474
$[Hg(Lb)_2]$	1666	1620	1558	665 642	457

Table 3: The values of magnetic sensitivity and electronic spectral of complexes.

Compound	*μeff. BM. exp.*	*λ (nm)*	*Ú cm^{-1}*	*Ɛmax molar^{-1} cm^{-1}*	*Assignments*
$[Co(Lb)_2]$	2.66	299 363 430 660	33444 30303 23255 15151	3890 3992 4 2	LF LF CT $^4T_{1g}\rightarrow{}^4A_{2g}$
$[Cu(Lb)_2]$	1.74	234 355 448 625	42735 28169 22321 1600	3619 4000 1779 4	LF LF CT $^2Eg\rightarrow{}^2T_{2g}$
$[Cd(Lb)_2]$	—	225 329 451	952 40000 4	952 40000 4	LF LF CT
$[Hg(Lb)_2]$	—	349 430	28653	3989	L.F C.T

due to the stretching frequency of the (HC=N) of the Lb, which shifted significantly in complexes compared to their frequency in the L at the site. 1672 cm^{-1}, which results in symmetry between the metal and the nitrogen atom as a donor atom.[17,18] The complexes spectra also showed a shift in position (1620–1618) for the group (C=N) ring, which indicates the consistency of the two nitrogen atoms in the imidazole ring with the atoms of the central ion.[19] The infrared spectrum of the complexes did not show the hydroxyl group, which appeared in the spectrum of the free ligand at the frequency 3471 cm^{-1}. This is evidence of the symmetry between the oxygen atom of the hydroxyl group (OH) and the metal ions.[20] In addition, the new absorption bands in complexes spectra, appear in the range

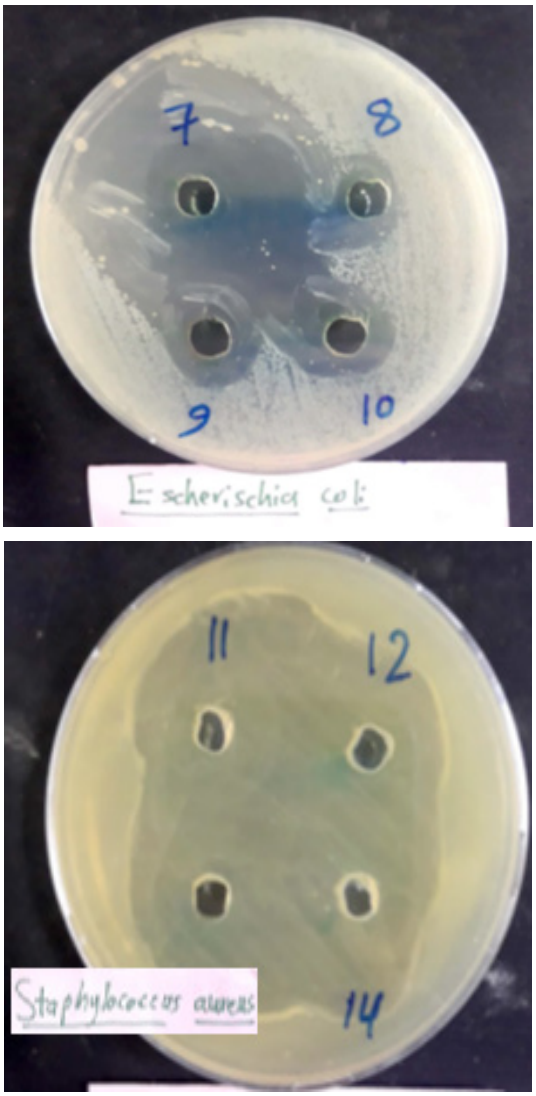


Chart 1: The inhibitions zone of the compounds

(474–455) cm^{-1}, (671–665) cm^{-1}, and (646–622) cm^{-1}, due to stretching vibration of (M-O) and (M-N) of the N-Schiff base group, and (M-N) for N- ring, respectively.[21]

The Magnetic sensitivity and Electronic Spectral

The Magnetic sensitivity of the cobalt and copper complexes 2.66 and 1.74 showed that they have paramagnetic properties. The UV-vis spectrum of the LB appeared peaks at (296 and 318) nm, which due to π →π* and 398 nm due to n→ π * transition.[22,23] Electronic spectra of complexes in Table 3 reveal peaks at (270–280) nm due to ligand field. The electron spectrum of the cobalt complex showed four absorption peaks at 299 nm, 363 nm, 430 nm, and 660 nm due to the ligand field spectrum, charge transmission spectrum, and ^4T_1g (F)→ ^4A_2g, respectively. The copper complex showed the first and second absorption peaks at 234 nm and 355 nm belonging to the ligand field region, and the third 448 nm back to the charge transfer region, while the fourth peak appeared at 625 nm refers to the electronic transmission $^2Eg \rightarrow {}^2T_2g$. The region of the ligand field appeared for the cadmium and mercury

Table 4: The inhibiting zone effect on bacteria.

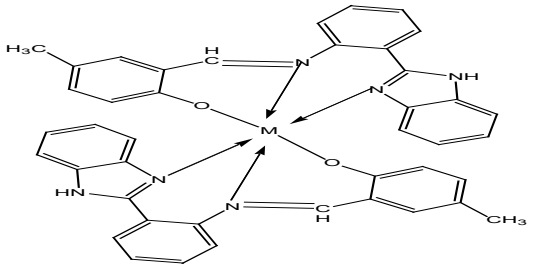
Comp.		*Staphylococcus aureus*	*Escherichia Coli*	*Rhizopodium*
7	Hg-2	48	23	40
8	Cd-2	18	0	13
9	Co-2	20	0	9
10	Cu-2	20	19	14
11	Lb	25	30	15
12	DMSO	20	30	13
14	Ampicillin	40	28	---

complexes at (329, 225) nm and 349 nm, respectively, while the region of transmission of the charge spectrum appeared at the wavelengths of 430 nm and 451 nm, respectively.[24-26]

Antibacterial Activities

In this study, all prepared compounds have been evaluated *in-vitro* as microorganisms of one type of gram-positive *S. aureus*, gram-negative bacteria *E. coli,* and *Rhizopodium* as fungus; however, the compounds have an excellent inhibiting effect on microorganisms, Lb and complexes against gram-negative, fungus, and gram-negative except for Co and Cd complexes, the reason is due to "Tweedy's" chelation theory in the complexes, the polarity of the metal ion will be reduced to a greater extent leads to the overlap of the ligand orbital and partial sharing of the M^{+2} with donor groups, the delocalization of (π electrons) over the whole chelate ring and the large ring size of ligands moiety makes the complexes more lipophilic in Table 4.[27-30]

CONCLUSIONS



where M= Co(II), Cu(II), Cd(II) and Hg(II)

The new Schiff base (E)-2-(((2-(1H-benzo[d]imidazol-2-yl) phenyl)imino)methyl)-4-methylphenol with some metal ions such as, Co(II), Cu(II), Cd(II) and Hg(II) was preparation and diagnosed. The results indicated that the ligand Schiff base was coordinated with the metal ions via nitrogen (imine group), nitrogen imidazole ring, and oxygen (phenolic group), the proposed form of complexes is octahedral geometry.

ACKNOWLEDGMENT

The authors express sincere appreciation to the chemistry department in my college of education for pure sciences Ibn Al Hitham, University of Baghdad, Iraq for their cooperation in completing this work.

REFERENCES

1. Gravatt GL Baguley, Bc Wilson. "Synthesis and antitumor activity of DNA minor groove-targeted aniline mustard analogues of pibenzimol". J.Med.Chem 1994;37:4338. http://dx.doi.org/10.1021/jm00051a010
2. M. Gabaa, P. Gabaa, D. Uppala, N. Dhingrac, MS. Bahiad O. Silakarid C. Mohan,"Benzimidazole derivatives'': search for GI-friendly anti-inflammatory analgesic agents,Acta. Pharm. Sin B. 2015;5:337-342.
3. SAH. El-Feky, ZKA. El-Samii, NA. Osman J. Lashine, MA. Kamel HK. Thabet, "Synthesis, molecular docking and anti-inflammatory screening of novel quinoline incorporated pyrazole derivatives using the Pfitzinger reaction II", Bioorg. Chem. 2015;58:104-116.
4. Kankate RS, Gide PS, Belsare DP. Design, synthesis and antifungal evaluation of novel benzimidazole tertiary amine type of fluconazole analogues. Arabian Journal of Chemistry. 2019 Dec 1;12(8):2224-2235.
5. C. W. Evans, C. Atkins, A. Pathak, B. E. Gilbert, J. W. Noah, "Benzimidazole analogs inhibit respiratory syncytial virus G protein function'', Antiviral. Res. 121 (2015) 31-38.
6. Sharma MC, Sharma S, Sahu NK, Kohli DV. 3D QSAR kNN-MFA studies on 6-substituted benzimidazoles derivatives as nonpeptide angiotensin II receptor antagonists: a rational approach to antihypertensive agents. Journal of Saudi Chemical Society. 2013 Apr 1;17(2):167-176.
7. Guigón-López C, Vargas-Albores F, Guerrero-Prieto V, Ruocco M, Lorito M. Changes in Trichoderma asperellum enzyme expression during parasitism of the cotton root rot pathogen Phymatotrichopsis omnivora. Fungal biology. 2015 Apr 1;119(4):264-273.
8. Paul A, Gupta RK, Dubey M, Sharma G, Koch B, Hundal G, Hundal MS, Pandey DS. Potential apoptosis inducing agents based on a new benzimidazole schiff base ligand and its dicopper (II) complex. RSC advances. 2014;4(78):41228-41236.
9. Kumar, A., Kumar, A., Dubey, M., Biswas, A., & Pandey, D. S. (2015). Detection of copper (II) and aluminium (III) by a new bis-benzimidazole Schiff base in aqueous media via distinct routes. RSC advances, 5(108), 88612-88624.
10. Magd-El-Din AA, Mousa HA, Labib AA, Hassan AS, Abd El-All AS, Ali MM, El-Rashedy AA, El-Desoky AH. Benzimidazole–Schiff bases and their complexes: synthesis, anticancer activity and molecular modeling as Aurora kinase inhibitor. Zeitschrift für Naturforschung C. 2018 Nov 1;73(11-12):465-478.
11. Lotfi A. Synthesis and characterization of novel mixed complexes derived from 2-aminomethylbenzimidazole and 2-(1H-Benzimidazol-2-yl) aniline and theoretical prediction of toxicity. Egyptian Journal of Chemistry, 2020;63(12), 4757-4767.
12. Ismail MF, Ei-Khamry AM, Hamid HA, Emara SA. Behaviour of 2-subst1tuted 6, 8-dibromo-3, 1-benzoxazin-4-ones towards o-phenylenediamine and anthranilic acid; a case of unusual cleavage of 6, 8-d1bromo-2-methyl-3, 1-benzoxazin-4-one. Tetrahedron. 1988 Jan 1;44(12):3757-3760.
13. Gary HG. Sharma RA.,J. Pharm. Sci., 1970,59:1691.
14. Mendham, J., 2006. Vogels textbook of quantitative chemical analysis. Pearson Education India.
15. Silverstein RM. Bassler GC. Spectrometric identification of organic compounds. Journal of Chemical Education, 1962;39: 546.
16. Ovas Ahmad Dar, Shabir Ahmad Lone, Manzoor Ahmad Malik, Mohmmad Younus Wani Aijaz Ahmad and Athar Adil

Hashmi, New transition metal complexes with a pendent indole ring: insights into the anti-fungal activity and mode of action, RSC advances, 2019;9:15151-15157.

17. Nakamoto K. Infrared spectra of inorganic and coordination compounds. 1970.
18. Sahib SK. Karem LKA. Some Metal Ions Complexes Derived From Schiff Base Ligand with Anthranillic Acid: Preparation, Spectroscopic and Biological Studies. Baghdad Science Journal, 2020l;17:99-105.
19. Alam, SAMF, Ahmad T, Nazmuzzaman M, Rahman S, Ray SK, Sharifuzzaman et al. Synthesis of benzimidazole derivatives containing schiff base exhibiting antimicrobial activities. International Journal of Research Studies in Biosciences (IJRSB), 2017;5(7).
20. Aziz MR. Synthesis and anti-bacterial study of the ligand type Schiff base derived from amino acid [L-Phenylalanine] and its complexes with Co (II), Ni (II), Cu (II) and Zn (II) ions. Ibn AL-Haitham Journal For Pure and Applied Science, 2017;23(2), 76-88.
21. Lotfi A. Synthesis and characterization of novel mixed complexes derived from 2-aminomethylbenzimidazole and 2-(1H-Benzimidazol-2-yl) aniline and theoretical prediction of toxicity. Egyptian Journal of Chemistry, 2020;63(12), 4757-4767.
22. Lever AP. Inorganic electronic spectroscopy. Studies in physical and theoretical chemistry, 1984;33.
23. Mahdi, SH, Karem LKA. Spectroscopic, Structural and Anti-bacterial Activity of Mixed Ligand Complexes from Schiff Base with Anthranilic Acid. Journal of Physics: Conference Series, IOP Publishing, 2019; 012089.
24. Naji SH, Karem LKA. Mousa, FH. Synthesis, Spectroscopic and Biological Studies of a New Some Complexes with N-Pyridin-2-Ylmethyl-Benzene-1, 2Diamine. Ibn AL-Haitham Journal For Pure and Applied Science, 2017;26:193-207.
25. Karem LKA Jaafar WA. Synthesis, Characterization and Biological Activity of Schiff Bases Chelates with Mn (II), Co (II), Ni (II), Cu (II) and Hg (II). Baghdad Science Journal, 2017; 4:390-402.
26. Mumtaz A, Mahmud T, Elsegood M, Weaver G, Bratu G, Mitu L. Synthesis, Characterization and Biological Evaluation of Schiff Base (N-4-(thiophene-2-yl-methyleneamino)-2, 6-dimethylpyrimidine-4-yl) benzenesulfonamide and its Complexes with Cu (II), Ni (II), Co (II), Fe (II), Mn (II), Zn (II) Ions. Revista De Chimie, 2020;71,206-212.
27. Karem LKAH. Synthesis, Spectral and Bacterial Studies of Mixed Ligand Complexes of Schiff Base Derived from Methyldopa and Anthranilic Acid with Some Metal Ions. Ibn Al-Haitham Journal for Pure and Applied scienc, IHSCICONF. 2017;1797:240-252.

28- Tweedy B. Plant extracts with metal ions as potential antimicrobial agents. Phytopathology, 1964;55:910-914.

29. Srivastava K, Singh SK, Mishra BP. L-1β, IL-1Ra and IL-18 gene variants in type 2 diabetes. Journal of Chemical and Pharmaceutical Research, 2015;7:197-203.
30. Neelakantan M, Esakkiammal M, Mariappan S, Dharmaraja J, Jeyakumar T. Synthesis, characterization and biocidal activities of some schiff base metal complexes. Indian Journal of Pharmaceutical Sciences, 2010;72:216.