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Synthesis and Antibacterial Activity of Schiff Base Compounds Derived from Glyoxal, Vanillin with Their Complexes with Iron (ш)

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Abstract

In this study, a library of Schiff bases derived from aliphatic (Glyoxal) and aromatic (Vanillin) aldehydes with different substituted aniline compounds. In addition to their complexes with Iron (III) were synthesized. The synthesized compounds were characterized by chemical and physical techniques (FTIR, ^{1}H-NMR, melting point, color, UV-Visible). The library of the Schiff bases and their complexes were tested against two types of human pathogen bacteria (*Staphylococcus aureus* (Gram-positive) and *Escherichia coli* (Gram-negative)). in a public way, The Fe^{+3} complexes were relatively more active against *Escherichia coli* than the corresponding Schiff bases. The antibacterial activities of the Schiff bases and their complexes against *Staphylococcus aureus* were variable.

Keywords: Antibacterial; Glyoxal; Schiff bases; Vanillin; Metal Complexes.

1. Introduction

Schiff bases are a special type of ligand that consists of the azomethine group (-C=N-) with different atoms and donations that give important types of harmony to different elements. The azomethine group (-C=N) might be responsible for biological activities associated with these compounds such as anti-tumors, antimicrobials, fungi, and active pesticides [1-5].

Schiff base is a multi-toothed ligand. It is designed is suitable for bonding element ions, opening sample space for preparing complexes with different elements [6, 7]. Like aggregates, it is easily prepared from the interaction of diamine with various types of salicylic aldehyde and its derivatives [8, 9]. Schiff base assemblies are known for their easy preparation, stability, and wide applications [10, 11]. The Schiff base is one of the most reported organic compounds with an integrated property and is widely used in the authorship of therapeutic agents [12- 14]. The process of preparing and diagnosing Schiff bases rules was studied in previous years in detail and large numbers [15-18]. There are many prepared Schiff bases from glyoxal, and vanillin and their metal complexes were studied their bioactivity [19,20].

Several compounds were prepared, as well as complexes of Schiff bases and elements. In this research, we have prepared several Schiff bases compounds and their complexes with Iron (III). Using of aliphatic (Glyoxal) and aromatic (Vanillin) aldehydes with different substituted aniline compounds. Then we studied their effect as antibacterial agents against two types of human pathogen bacteria (*Staphylococcus aureus (Gram-*positive) and *Escherichia coli* (Gram-negative). At the same time, ferric Schiff base complexes were prepared with some minerals and studied their effect against the same type of two bacterial *Escherichia coli* and *Staphylococcus aureus*

2. Experimental section

2.1. Instrument

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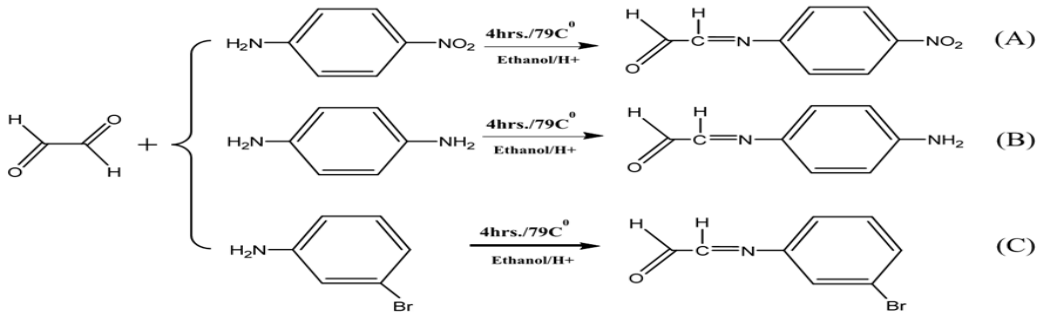
Glyoxal, vanillin, p-nitro aniline, m-bromoaniline, and p-phenylenediamine were purchased from Merck and used as received without any further purification. Other solvents and reagents were used as analytical grade and purchased commercially. FTIR spectra (KBr discs) were recorded on a JASCO FTIR 4200 instrument, with a wavenumber range of (400-4000) cm^{-1}. The electronic spectra were measured in the range of 200 - 1100 nm by using Absolute ethanol solvent by using UV-Visible spectrophotometer type Shimadzu UV-160A using a quartz cell of (1.0 cm) length. ^{1}H-NMR is recorded using Bruker 500 MHz available at Tehran University.

2.2. Synthesis

2.2.1. Preparation of Schiff bases A, B, and C :

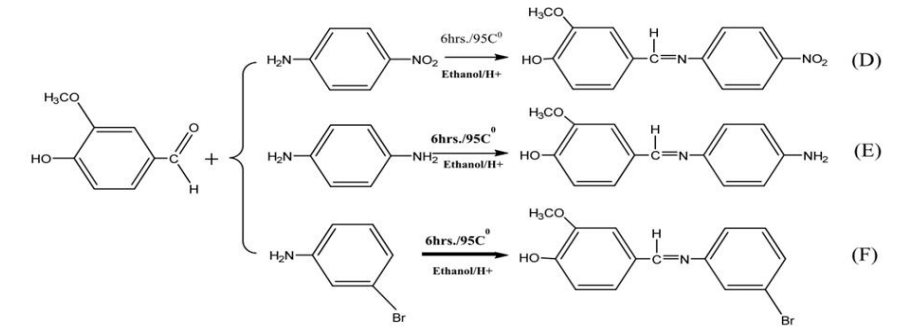
Schiff base A was prepared according to the following procedure [21] (Scheme 1). A 0.967 g of p-nitro aniline (0.007 moles) was dissolved in 30 mL of ethanol. The mixture was heated. After that to 73°C, a 30 mL of (0.407 g) glyoxal (0.007 moles) in ethanol was added under constant stirring. Then, a few drops of glacial acetic acid were added and the mixture was refluxed at (79±5 °C) for 4 hrs. The mixture was cooled down. Then a yellow precipitate was precipitated out. After that, the product was filtered and washed with cold ethanol. The product was recrystallized using ethanol. The same method was used to prepare Schiff bases (B and C).



Scheme (1): Preparation of A, B, and C Schiff Bases

2.2.2.Preparation of Schiff bases D, E, and F :

Schiff base D was prepared according to the following procedure[(scheme 2). A 0.967 g of p-nitro aniline (0.007 moles) was dissolved in 50 mL of ethanol. The mixture was heated. After that to 88oC, a 50 mL of 1.065 g of vanillin (0.007 moles) in ethanol was added under constant stirring. Then, a few drops of glacial acetic acid were added and the mixture was refluxed at (95±5 °C) for 4 hrs. The mixture was cooled down. Then a pale orange precipitate was precipitated out. After that, the product was filtered and washed with cold ethanol. The product was recrystallized using ethanol. The same method was used to prepare Schiff bases(E and F).



Scheme (2): Preparation of D, E, and F Schiff Bases.

2.2.3. Synthesis of Metal Complexes

The metal complexes were prepared by reaction of Schiff bases (1 mol) in 30 ml of ethanol with (1 mol) with the $FeCl_3$ salt. The mixture was heated under reflux for 4 hrs. The resulting solution was concentrated to (1/2) of it is volume and cooled down to (25°C). The precipitated complex was filtered then washed with ethanol and dried over $CaCl_2$. Resulting the Schiff base-Fe^{+3} complexes: A- Fe^{+3}, B-Fe^{+3}, C-Fe^{+3}, D- Fe^{+3}, E- Fe^{+3}, and F- Fe_{+3} complexes.

3. Results and Discussion Results and Discussion

3.1. UV spectra

The UV spectra of the Schiff bases shows different broad bands at (~355 and ~418) nm due to the various electronic transition. The absorption maxima of the Fe^{+3} chelate close resemblance with the free Schiff base and the band values were at (356-587.3) nm, The values shifted slightly to longer wavelength signalize the participation of the azomethine groups(-C=N) in metal complexation. Table (1) shows important wavelengths and absorption. The gangs are due to transformations within the legend. The peaks observed below 350 nm are initially assumed due to transitions $\pi \rightarrow \pi^*$, $n \rightarrow \pi^*$ and $n \rightarrow \sigma^*$. Summits above 350 nm are assumed to be due to charge transfer.

Ligands	U.V. λ_{max} (nm)	Complexes	U.V. λ_{max} (nm)
A	395	A- Fe^{+3}	408 433 420
B	390	B- Fe^{+3}	434 356
C	418	C- Fe^{+3}	429 454
D	359	D- Fe^{+3}	451
E	403	E- Fe^{+3}	587.3
F	355	F- Fe^{+3}	452.7

Table (1). Absorption peaks of UV spectra.

3.2. ^{1}H-NMR Spectra

The compounds were diagnosed with the ^{1}H-NMR using dimethyl sulfoxide-D6 (DMSO) as a solvent. The ^{1}H-NMR spectrum of compounds D and E showed a singlet beak at 3.8 ppm for the proton of methyl groups (CH_3-O). The protons of the aromatic ring are also observed at (6.9-7.2) ppm. The singlet beak at 8.5 ppm was diagnosed for the proton of the amides and the signal at 7.5 ppm is assigned to the amino groups in (E). The signal at (2.5) ppm is assigned to the proton of the OH group for (D and E). The band belongs to the azomethine group at (8.4) ppm and signals around (6.5-7.2) ppm are attributed to the protons of aromatic rings and. Compounds (A and B) contain an aldehyde group, the aldehydic proton for compounds(A and B) (which is expected to appear at δ 9.7 –10 ppm is missing in the^{1}H-NMR spectra. That probably suggests that the two aldehydic hydrogens of the glyoxal reacted and involved in the formation of the obtained Schiff base,

as well as the disappearance of the amine group band in the compound (B and E), which means that the reaction of the formation of the azo-methene group.

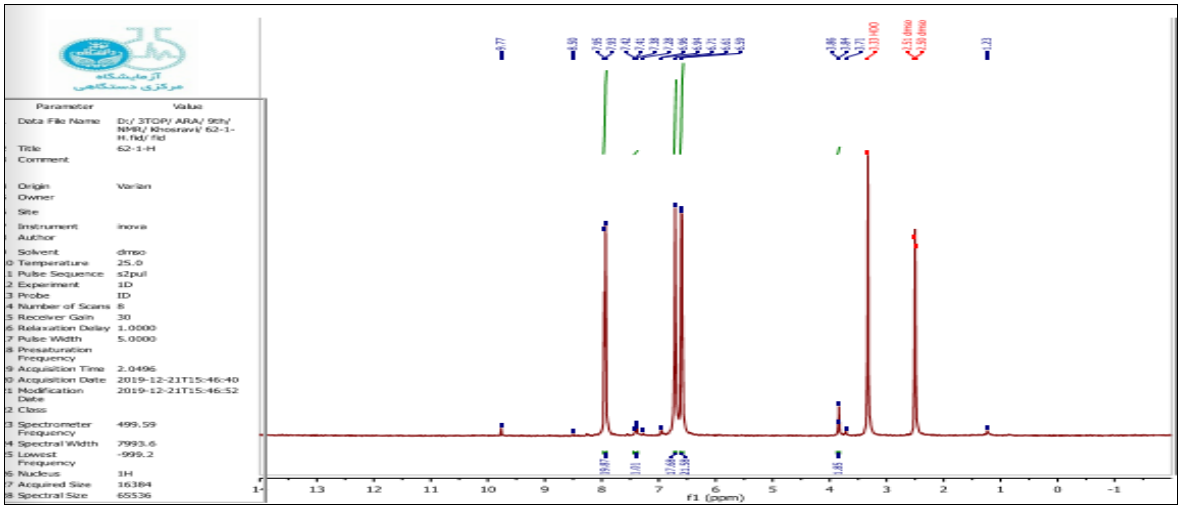


Figure 1: ^{1}H-NMR (A) Ligand.

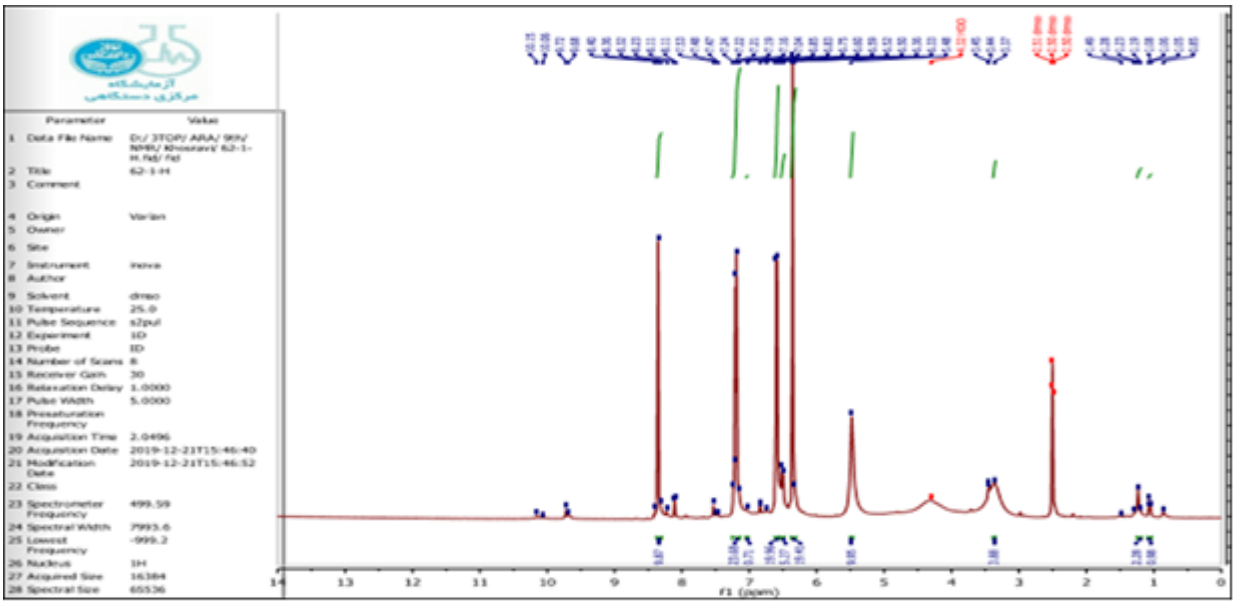


Figure 2: ^{1}H-NMR of (B) Ligand.

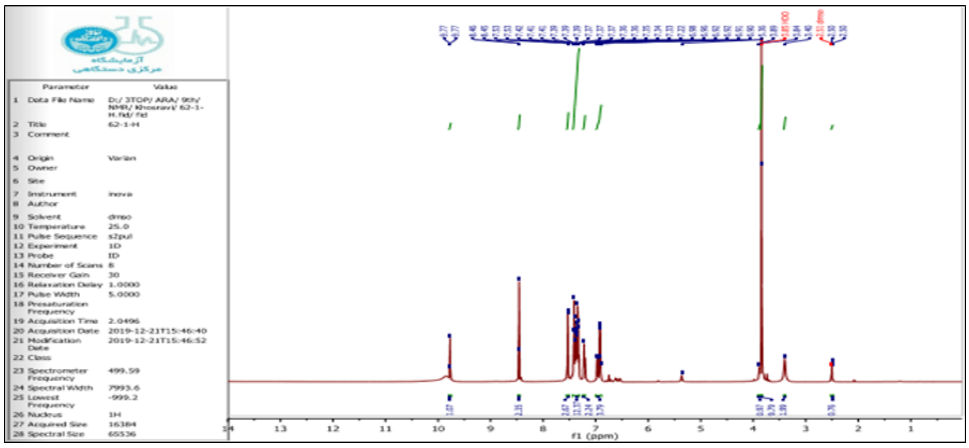


Figure 1: ^{1}H-NMR (D) Ligand.

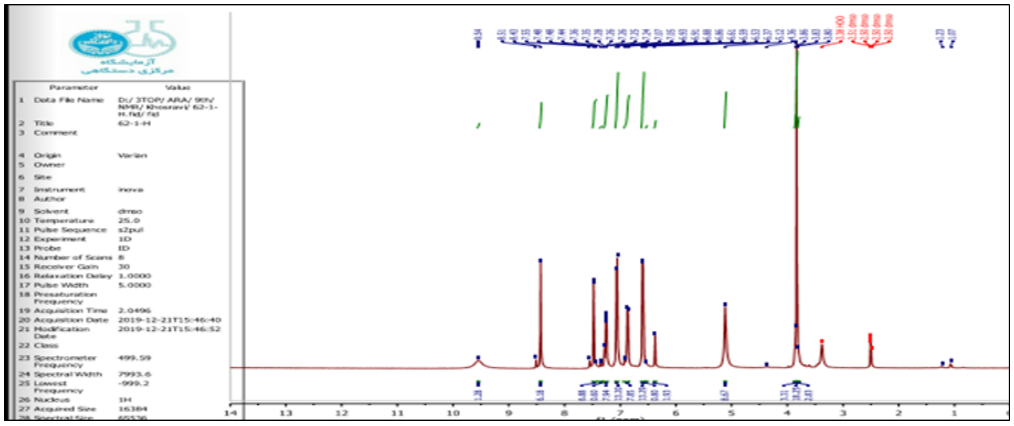


Figure (4): ^{1}H-NMR (E) Ligand.

3.3.FTIR Analysis.

The spectra of the Schiff bases gave two strong peaks at 1620 and 1422 cm^{-1} due to asymmetric and symmetrical azomethine group groups in the compounds. The absorption bands manifest at 1016 cm^{-1} and 2923 cm^{-1} belonged to (C–O) and (aliphatic C–H) stretching vibrations. The bands in 1400–1500 cm^{-1} and 3500–3000 cm^{-1} represented ($–CH_2$) stretching vibrations and (–OH) groups of Schiff bases, respectively Table 2 showed the important peaks of the prepared Schiff bases.

Schiff Bases	Physical State	m.p. ° C (dec.)	Yield%	Assignment		
				υ (O-H) cm^{-1}	υ (CH_2) cm^{-1}	υ (C=N) cm^{-1}
A	yellow powder	66-68	86.61	3751,3637	2887, 2828	1668
B	brown powder	71-74	90.66	3416	2955, 2715	1634

C	brown viscose	-	85.5	3374	2805, 2889	1594
D	orange powder	160-162	70	3381	2840	1675
E	brown powder	182-185	86.35	3473	2584	1623
F	Dark brown powder	148-150	84.53	3374	2289	1594

Table (2): Physical properties and Infrared characteristic bands frequencies (cm^{-1}) of the prepared Schiff base ligands.

3.4. Antibacterial Evaluation

All the synthesized Schiff bases and their Fe^{+3} complexes were selected for antimicrobial activity screening using a disk diffusion treatment against at least one of the two bacterial strains used during the testing [22,23]. For the diffusion treatment Weii-Variant, the solvent was used as dimethyl sulfoxide (DMSO), and for the remaining methodologies, suitable solvents were used for the dissolution of Schiff bases and Fe^{+3} complexes. The antibacterial activity of Schiff bases and the Fe^{+3} complexes were assessed against two kinds of bacteria species: Staphylococcus aureus and Escherichia coli. After 24 hrs. of incubation, bacterial suspension was diluted with sterile physiological solution, for the diffusion presses, to 108 CFU/ml (turbidity=McFarland barium sulfate standard 0.5).

3.4.1. Agar Diffusion Well Variant.

Bacterial vaccines spread uniformly using a sterile cotton swab on a sterile Muller Hinton Agar (MHA) Petri dish. A 50 ml of a 100 mg/mL of Schiff bases and Fe^{+3} complexes were added to each well (holes of 7 mm in gel agar and drainage). The dishes were incubated for 24 hours at 37° C under aerobic conditions. After incubation, the growth of undulating bacteria is observed. The inhibition of bacterial growth was measured in mm.

3.4.2. Results of the Biological Activity

The biological activity of the Schiff bases and their Fe^{+3} complexes are shown in the figures (5-10). The Fe^{+3} complexes were more active against S. aureus than the Schiff bases alone. The Fe^{+3} complexes and Schiff bases inhibition diameters were ranged between (20-24) mm and (15 -30) mm respectively. On the other hand, the inhibition diameters against Escherichia coli for the Schiff bases and their Fe^{+3} complexes were variable. It was ranged (12-30) mm for the Schiff bases, and (16- 30) mm for their Fe^{+3} complexes. The Fe^{+3} complexes were relatively more active against Escherichia coli than the corresponding Schiff bases. The antibacterial activities of the Schiff bases and their complexes against Staphylococcus aureus. were variable. The assortment degree of activity listed against gram-positive and gram-negative bacteria is shown in table *(3).*

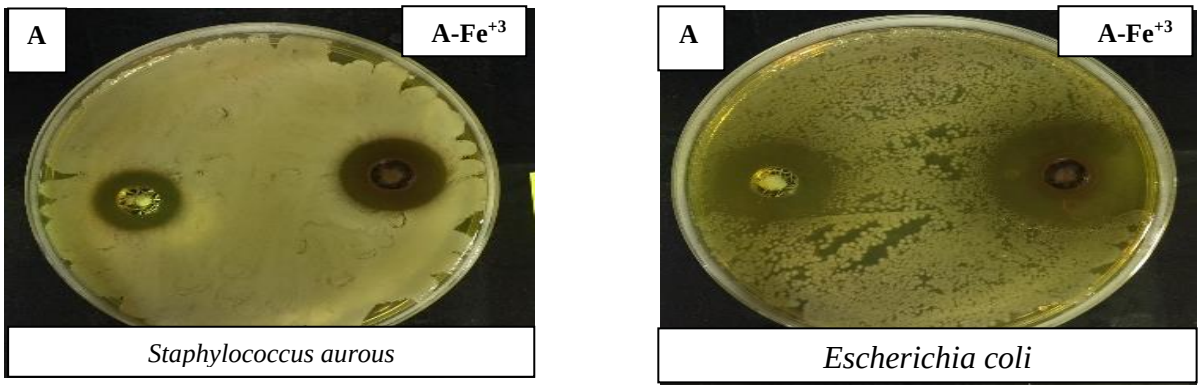


Figure (5): Show zone of inhibition of ligand A and its Fe^{+3} complex against *Staphylococcus aureus*.and *Escherichia coli* Bacterias. (A).

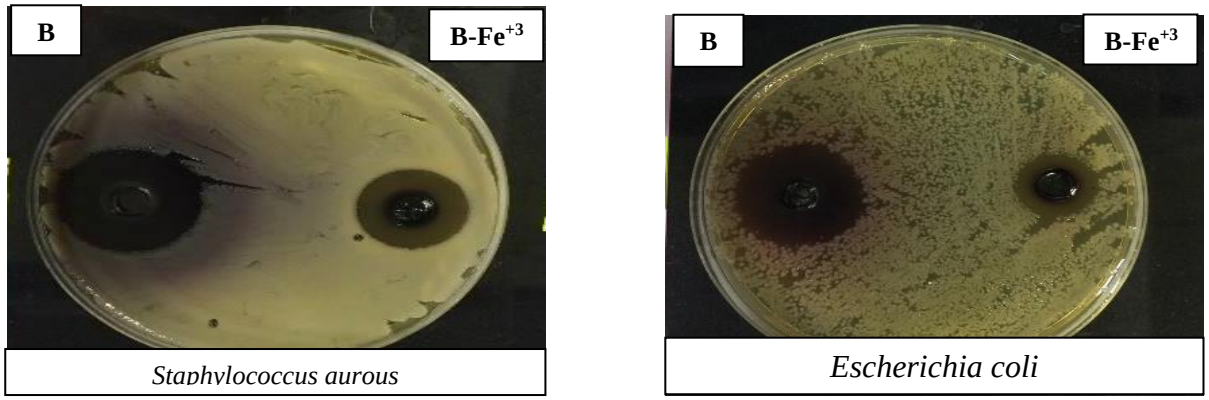


Figure (6): Show zone of inhibition of ligand D and its Fe^{+3} complex against *Staphylococcus aureus*.and *Escherichia coli* Bacterias. (B).

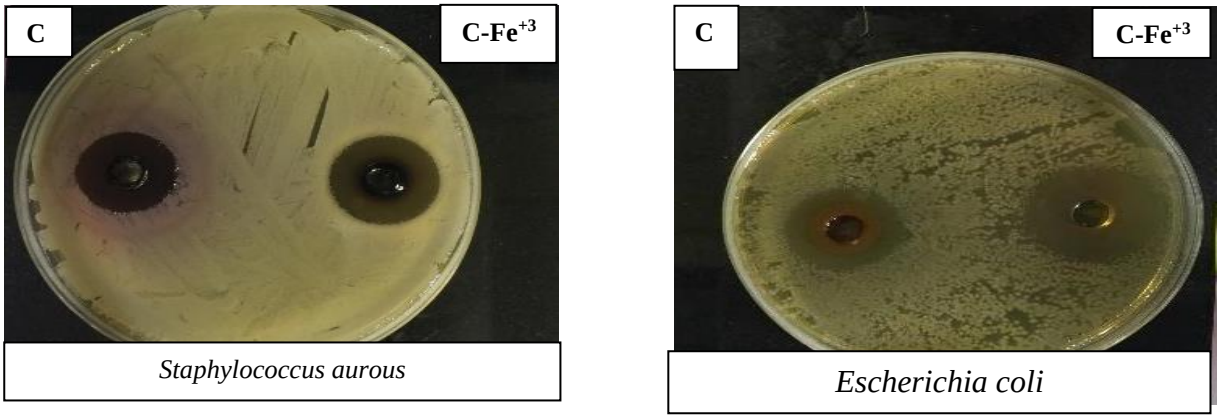


Figure (7): Show zone of inhibition of ligand F and its Fe^{+3} complex against *Staphylococcus aureus*.and *Escherichiaacoli* Bacterias. (C).

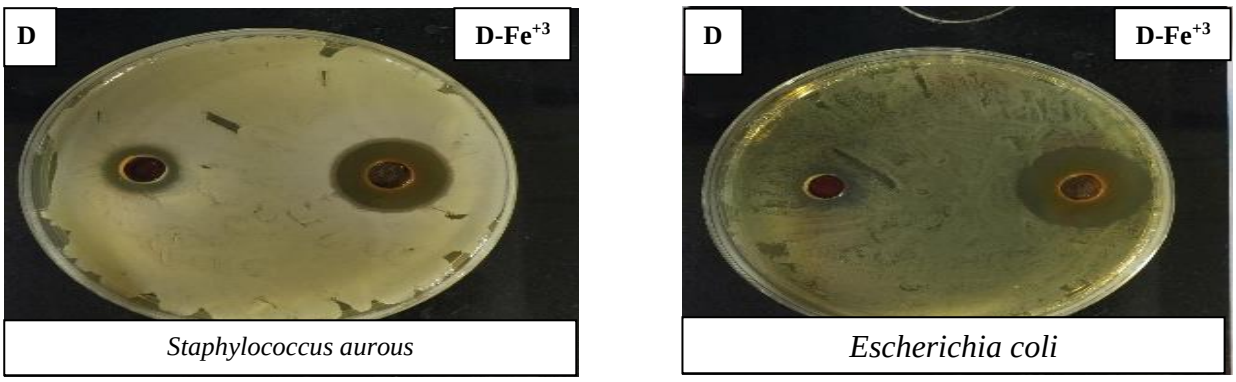


Figure (8): Show zone of inhibition of ligand E and its Fe^{+3} complex against *Staphylococcus aureus*.and *Escherichia coli* Bacterias. (D).

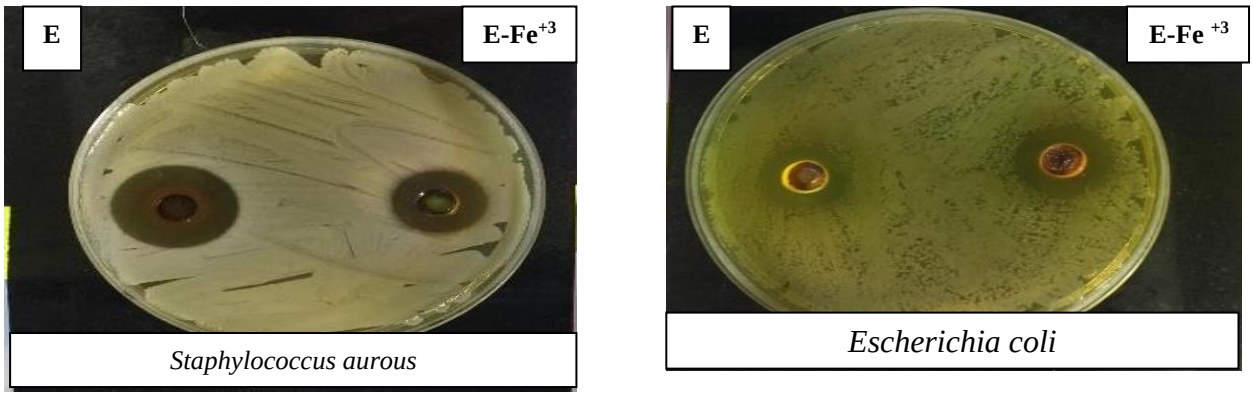


Figure (9): Show zone of inhibition of ligand B and its Fe^{+3} complex against *Staphylococcus aureus*.and *Escherichia coli* Bacterias. (E).

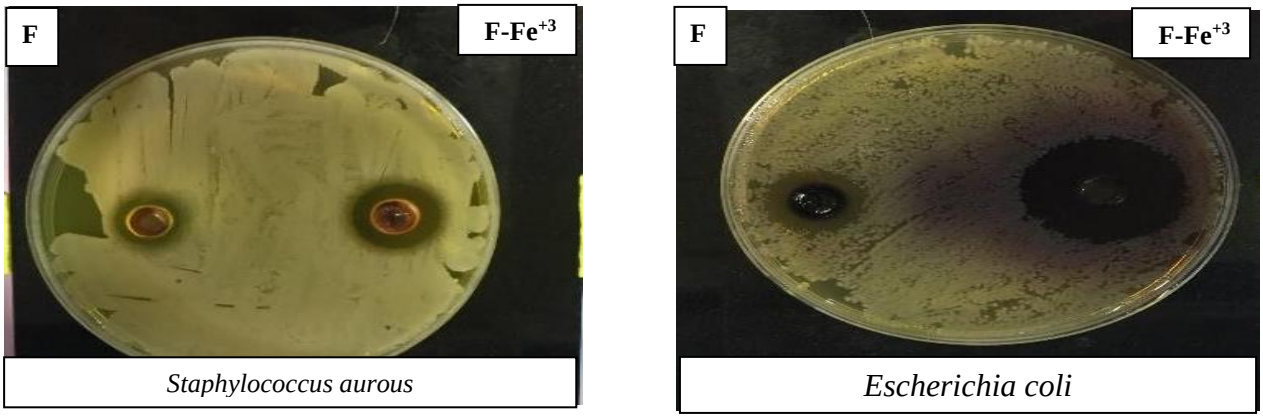


Figure (10): Show zone of inhibition of ligand C and its Fe^{+3} complex against *Staphylococcus aureus*. and *Escherichia coli* Bacterias. (F).

Schiff Bases and Fe^{+3} Complexes	Inhibition Zone(mm)	
	Escherichia coli	*Staphylococcus aureus*.
A	**16**	**22**
A-Fe^{+3}	***20***	***30***
E	***30***	***30***
E-Fe^{+3}	***21***	***20***
D	***20***	***30***
D-Fe^{+3}	***24***	***24***
F	***15***	***12***
F-Fe^{+3}	***20***	***25***
B	***20***	***25***
B-Fe^{+3}	***21***	***16***
C	***15***	***16***
C-Fe^{+3}	***20***	***20***

Table (3): show the Inhibition Zone (mm).

4. Conclusion:

Schiff bases have been prepared by the condensation of Glyoxal and Vanillin with different substituted Aniline. FTIR, ^{1}H-NMR, and UV-Visible spectroscopy, measurements confirm the structures of the synthesized Schiff bases and their Iron (III) complexes. Antimicrobial screening tests were

performed against two kinds of bacteria *Escherichia coli and Staphylococcus aureus.* The comparative study of the antibacterial inhibition values of the Schiff bases and their Fe^{+3} complexes indicate that the Fe^{+3} complexes exhibit greater antibacterial activity than the free ligand. The association of azomethine in the Schiff bases is responsible for the biological activities of antibacterial activities. Schiff bases connect with the Iron ion in certain ways to give another efficacy either less or more than the Schiff bases.

References

1-**Muhammed Aqel Ashraf, Karamat Mahmood, and Abdul Wajid**. Synthesis, Characterization, and a Biological Activity of Schiff Bases" International Conference on Chemistry and Chemical Process. Vol. 10. (2011).

2-**Gehad Geindy Mohamed, Mohamed Mohamed Omar, and Ahmed Mohamed Hindy**. Metal Complexes of Schiff Bases: Preparation Characterization, and Biological Activity: Turk J. of Chem. 30, 361-382 (2006).

3 -**M.S Mohy Eldin, A. I. Hashem, A. M. Omer, and T. M. Tamer** "Preparation, Characterization and antimicrobial evaluation of novel cinnamyl chitosan Schiff base" International J. of Advanced Res. , 3,741-755(2015).

4-**Prashant Singh and Rajesh K.S. Dhakarey**, Synthesis, Characterization and antimicrobial studies of metal complexes with Schiff bases derived from 2-thienyl Glyoxal, Rasayan J.Chem., Vol.2, No.4),869-874.(2009).

5- **Khudheyer J Kadhim, Murad G. Munahi**, Synthesis, Characterization and Biological Evaluation of Some Novel Schiff'S Bases Derived from Vanillin, Journal of Global Pharma Technology, 10(9):383-386. (2017).

6 - **Sashikala S, S. Syed Shafi**. Synthesis, Characterization, and Antimicrobial activity of chitosan 4-chlorobenzaldebyde Schiff base Res. J. Chem. sci. 5(9), 27-33 (2015)

7- **Salih Hadi Kadhim, Ibtihal Qahtan Abd-Alla, and Thikra Jawad Hashim**. Synthesis and Characteristic Study of Co (II), Ni (II), and Cu (II) Complexes of New Schiff Base Derived from 4-Amino Antipyrine. Int. J. Chem. Sci. 15(1) 107(2017).

8- **L.V.Gavali, and P.P.Hankarep**. Synthesis and Characterization of the Complexes of some Transition Metals with 4-[2'-Hydroxy salicylidene -5(2" –thiazolyazo]Chlorobenzene. J. of Physical Sci.11, 147-155(2007).

9 -**A.Sahraei.H.Kargar, and M.Hakimi**. Applications and attributes of Nickel (II) Schiff base complexes derived from phenylenediamine. Bulgarian Chemical Communications, Special Edition F, 33-43, (2016).

10 -**Foziah A.Al-Saif**. Spectroscopic Elucidation, Conductivity and Activation Thermodynamic Parameters Studies on Pt (IV),Au(III) and Pd (II) 1,5-Dimethyl-2-phenyl-4-[(thiophene-2-yl-methylene)-amino]-1,1-dihydro-pyrazol-3-one Schiff Bases Complexes. International J. of Electrochemical. Sci. 9, 398-417(2014).

11 -**Muneera Fatin Manan, Karimah Kassim, Mohd Abdul Manan**. Synthesis, Characterization, and Conductivity Study of Schiff Ligand Derived from Isatin and O-Phenylenediamine with its Cobalt (11) Metal Complex and Lithium-Schiff Base Compound. The Malaysian J. of analytical Sci., Vol 16(3), 318-324(2012).

12 -**S. Sashikala, and S. Syed Shafi.** Synthesis, Characterization, and Antimicrobial activity of Chitosan vanillin Schiff bases. International J. of Novel Trends in Pharmaceutical Sci.7 (30), 86-92.ISSN: 2277-2782. (2017).

13 -**Sundaramurthy Santha Lakshmi, Kannappan Geetha, and P. Seenuvasa Kumaran**. Synthesis, Spectral and biological characterization of Schiff base transition metal complexes derived from L-tyrosine. J. of Chem. and Pharmaceutical Res. 8(3):823-830(2016).

14 -**Natiq G. Ahmed, and Hussein Y. Al-Hashimi**. Preparation and Characterization of some New Schiff Bases Compounds with the Study of Biological Effectiveness. Int. J. Curr. Res. Bio sci. Plant biol.. 3(5). 127-136 (2016).

15- **Wail Al Zoubi, Abbas Ali Salih Al-Hamdani, Susan Duraid Ahmed, and| Young Gun Ko.** Synthesis, characterization, and biological activity of Schiff bases metal complexes. J Phys. Org. Chem. 1-13(2017).

16- **Esmadi FT, Khabour OF, Abbas K, Mohammad AE, Obeidat RT, Mfady D**. Synthesis, characterization and biological activity of some unsymmetrical Schiff base transition metal complexes. Drug Chem. Toxicol. 39(1), 41-7(2016).

17- **Vhanale BT, Deshmukh NJ, and A T Shinde**. Synthesis, characterization, spectroscopic studies, and biological evaluation of Schiff bases derived from 1-hydroxy-2acetonapthanone Heliyon. 5(11), 1-18(2019)

18- **Eliene Leandro de Araújo, Hellen Franciane GonçalvesBarbosa, Edward RalphDockal, and Éder Tadeu GomesCavalheiro**. Synthesis, characterization, and biological activity of Cu (II), Ni (II), and Zn (II) complexes of biopolymeric Schiff bases of salicylaldehydes and chitosan. International J. of Biological Macromolecules.95,168-176(2017).

19-**Prashant Singh, Shanu Das, and Rajesh Dhakarey**, Bioinorganic Relevance of Some Cobalt(II) Complexes with Thiophene-2-glyoxal Derived Schiff Bases, E-Journal of Chemistry, 6(1), 99-105. (2009)

20-, **Yawen Xuan, Jiang Long Yin, and Li Shujie**, Synthesis and Characterization of a Novel o-Vanillin Schiff Base Derivatives and Their Complexes With Zn(II), Journal, Synthesis, and Reactivity in Inorganic, Metal-Organic, and Nano-Metal Chemistry, Volume 44, Issue 6, pages 877-880. (2014).

21-**Mala Nath, Rakesh Yadav**, Synthesis, Spectral and Thermal Studies of Fe(III), Co(II), Ni(II), Cu(II) and Zn(II) Complexes of Schiff Bases Derived from o-Aminobenzyl Alcohol, Journal Synthesis, and Reactivity in Inorganic and Metal-Organic Chemistry Volume 25, 1ssue 9. (1995).

22-**Smania A, Monache, F.D., Smania, E.F.A., and Cuneo. R. S**. Antibacterial activity of steroidal compounds isolated from Ganoderma applanatum (Pers.) Pat, (Aphyllophore-mycetideae) Fruit body.Int. J. Med. Mushrooms, 1,325-330(1999).

23-**Vanden Berghe, D. A., and Vlietinck A.J**. .Screening methods for antibacterial and antiviral agents from higher plants.In: Dey, P.M., Harbone, J, D. (eds), Methods in plant biochemistry, Academia Press, London, 47-69(1991).