Article

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Preparation. Identification and Antioxidant of some new Imidazolidine tetrazole, and thiazolidine derivatives from Schiff bases

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Abstract:

Several heterocyclic derivatives were developed for this study. The synthetic strategy was carried out in two stages: first, the preparation of three different types of derivatives of Schiff bases (F1-F3); It was prepared by reacting one mole of *p*-phenylenediamine with two moles of aromatic aldehydes (4-nitrobenzaldehyde, 4-(methylthio) benzaldehyde, 4-(pyridin-2-yl) benzaldehyde) .The second step was the formation of pent acyclic heterocyclic compounds (Imidazolidinone, tetrazole, and thiazolidinone) by reacting Schiff bases with different amino acids, sodium azide and thioglycolic acid. This is done by taking two moles of it to form five-ring heterocyclic derivatives (F4-F19). The progress of the reactions was monitored using TLC technology. The compounds were characterized using" FT-IR, H-NMR, and 13C-NMR spectra" techniques. The biological activity of some of the compounds bacteria Such as (*Escherichia coli* and *Staphylococcus aureus*), high efficacy against these bacteria. Antioxidant compounds were also studied, and then molecular docking investigations were performed using MOE software. Good binding interactions have been reported when using heterocyclic compounds (F10) as targets,

Keywords: Schiff bases, Imidazolidinone, thiazolidinone, biological activity

Introduction:

Schiff bases are carriers of the functional group known as imin, or azome mthine (-C = N -). That's condensation. primary amine products, such as carbonyl compounds and, initially, Higo Schiff. (1,3). Play the chemistry of the double bond between carbon and nitrogen an important role in the advancement of chemical sciences (4,7).

Imidazolidinone: - With the formula C3H8N2, Imidazolidinone is a heterogeneous five-ring compound (8). attracted notice due to its important responsibilities (9,13). as ingredients in the production of active chemicals (14, 18). Heterocyclic compounds containing (Imidazolidinone is the category of compounds good for their biological applications (18,19)

Tetrazoles: - are a type of artificial heterocyclic compounds that have two hydrogen atoms, one carbon atom, and four nitrogen atoms in a five-membered ring (Fig. 1). Tetrazole's chemical formula is CN4H2. Tetrazole is a crystalline substance that is pale yellow to white in color. It is soluble in alcohol or water and has a mild, distinctive smell. Due to the presence of four nitrogen atoms, it has an acidic character (20).

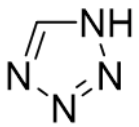


Fig. (1).

thiazolidinone:

A type of heterocyclic chemical compounds known as thiazolidinones has five members in a saturated ring, one thio ether group at position one and one amine group at position three. It is oxazolidine's sulfur counterpart. A condensation process between a thiol and an aldehyde or ketone can be used to create thiazolidines. This reaction is reversible. As a result, a large number of thiazolidines are hydrolyzable in aqueous solution. The thiol and aldehyde that were created during the thiazolidine's hydrolysis (21).

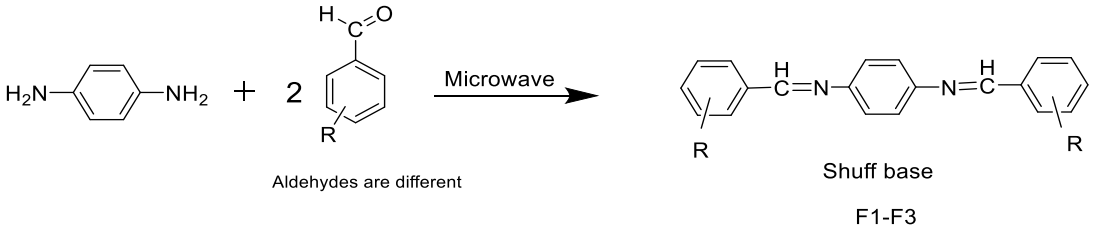
Materials And Methods

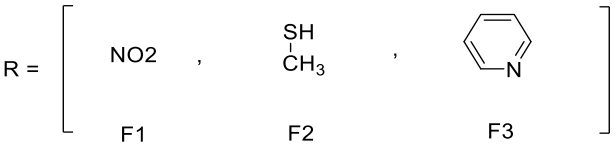
The purest chemicals were provided by Merck and Fluka-company. Melting point engineering LTD, U.K.'s electro thermal 9300 was used to measure and record melting points. Spots were visible by thin layer chromatography (TLC) on silica gel thanks to the use of iodine vapors. Using Bruker Ultra Shield 400 MHz Switzerland as the solvent, "FTIR" spectra, Fourier transform infrared shiatsu (8400), "1H-NMR, and 13C-NMR

spectra" in (ppm) unit were used (Iran). Newal ,Microwave Oven, Model NO. : MWO-261-01, 230-240 V ,50Hz,700W.

The general method for preparing Schiff base compounds(F1-F3).

The mixture of (p-phenene diamine) and other heterogeneous aromatic aldehydes included p-nitro benzaldehyde (1.398g, 0.008 mol), methyl thio benzaldehyde (1.216g, 0.008 mol), and pyridinyl benzaldehyde (0.732g, 0.008 mol). That is, the two components were thoroughly ground in a porcelain bowl at a ratio of 1:2 until their colors and shapes were uniform, then droplets of pure ethanol were added as a solvent. In a microwave oven, radiation was applied to the reaction mixture. After only 15 to 25 minutes, the reaction was finished, and the compounds' purity as well as the reaction path were seen using TLC ethanol:benzene (3:2) before the mixture was filtered and dried. and employed pure ethanol to recrystallize.





Scheme1: Synthesis of Schiff base compound

The general method for preparing Imidazolidinone compounds(F4-F15):

(0.1 g, 0.0002 mol) of Schiff bases (F1-F3) mixed with (0.0356 g, 0.0004 mol) of amino acids (alanine, phenylalanine, tyrosine, glycine) respectively, with the addition of 1 ml of dry gasoline as a solvent, and placed in a ceramic container. The materials are mixed until a dough is formed and then transferred to the microwave for (15-28) minutes, after irradiation is complete. The mixture was taken out and left to cool at laboratory

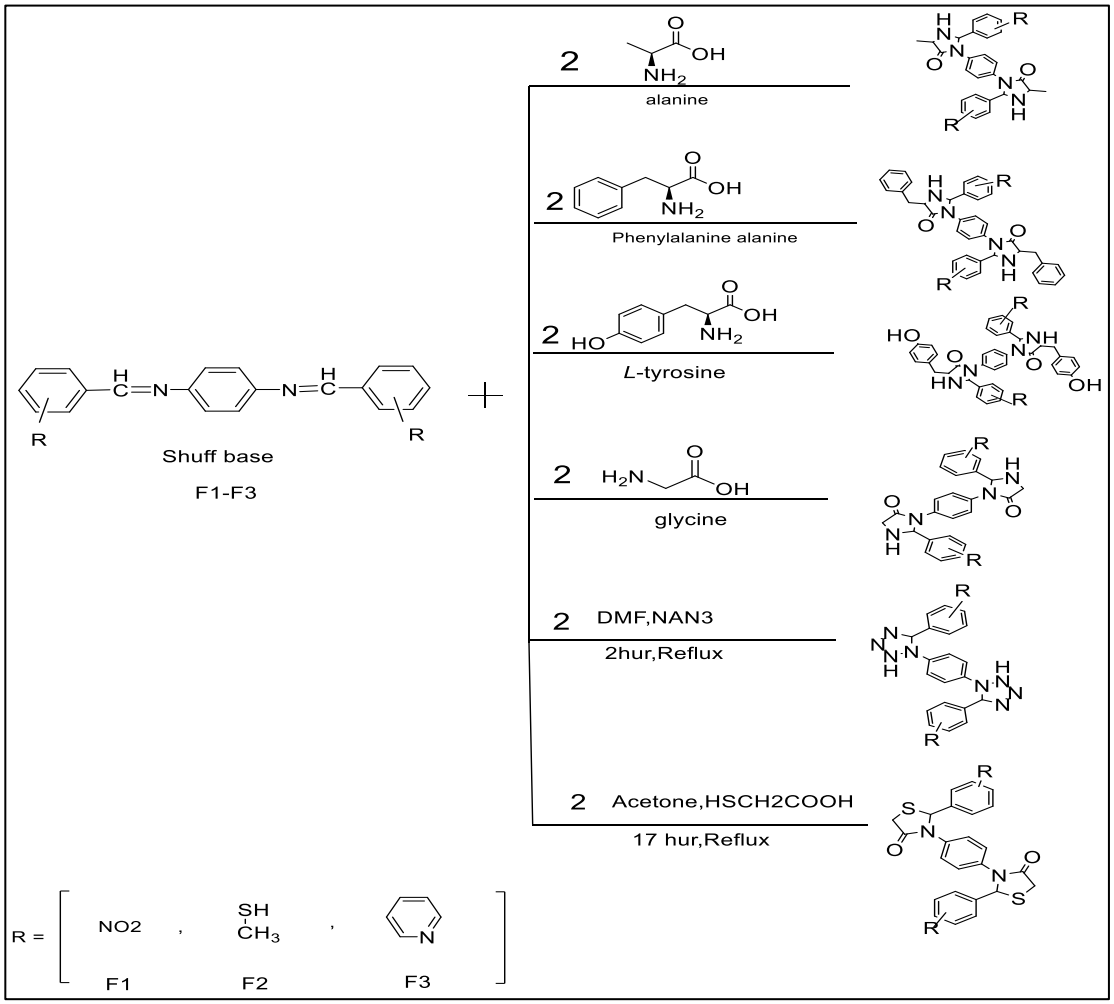
temperature. The resulting Product was washed with gasoline. Table 1 contains a list of the physical properties of these compounds

The general method for preparing tetrazol compounds(F16-F17):

(0.2 g, 0.0005 mol) of F1, F3 the previously prepared Schiff base, in 15 ml of DMF. We add to it (0.07 g, 0.0001 mol) NaN3 to, the mixture is placed for (21 hours) on the sublimation device, then follow of the reaction using the TLC technique (methanol: benzene (1:9) and it is recrystallized with absolute ethanol. To afforded prepare (F16), (F17).

The general method for preparing thiazolidinone compounds(F18-F19) (22):

(0.2 g, 0.0005 mol) of F1, F3 the previously prepared Schiff base, dissolved it in 15 ml



Scheme2: Synthesis of Five membered ring heterocyclic compounds

of Acetone. We add to it (0.095 g, 0.0001 mol) Thioglycolic acid (SHCH2COOH) to prepare(F18), (F19). The mixture is placed for (16 hours) on the sublimation device, then follow of the reaction using the TLc technique (methanol: benzene (1:9) and it is recrystallized with absolute ethanol.

Table (1). The physical properties of these compounds are listed in

%yield	color	Rf	M.P0^c	M.WT gm.\mol	M.F	Name of compound	No.
96	yellow	0.66	184-186	516.574	C26H24O6N6	3,3 '-(1,4-phenylene)bis(5-methyl-2-(4-nitrophenyl)imidazolidin-4-one)	F4
39	yellow	0.59	172-174	668.710	C38H32O6N6	3,3'-(1,4-phenylene)bis(5-benzyl-2-(4-nitrophenyl)imidazolidin-4-one)	F5
99	yellow	0.66	219-221	700.708	C38H32N6O8	3,3'-(1,4-phenylene)bis(5-(4-hydroxybenzyl)-2-(4-nitrophenyl)imidazolidin-4-one)	F6
80	yellow	0.65	191-193	488.460	C24H20N6O6	3,3'-(1,4-phenylene)bis(2-(4-nitrophenyl)imidazolidin-4-one)	F7
58	beige	0.78	209-211	518.694	C28H30N4O2S2	3,3'-(1,4-phenylene)bis(5-methyl-2-(4-(methylthio)phenyl)imidazolidin-4-one)	F8
83	beige	0.62	190-192	670.890	C40H38N4O2S2	3,3'-(1,4-phenylene)bis(5-benzyl-2-(4-(methylthio)phenyl)imidazolidin-4-one)	F9
88	Light beige	0.50	221-223	702.888	C40H38N4O4S2	3,3'-(1,4-phenylene)bis(5-(4-hydroxybenzyl)-2-(4-(methylthio)phenyl)imidazolidin-4-one)	F10
86	Dark beige	0.52	213-215	490.640	C26H26N4O2S2	3,3'-(1,4-phenylene)bis(2-(4-(methylthio)phenyl)imidazolidin-4-one)	F11
86	Greenish yellow	0.56	201-199	580.692	C36H32N6O2	3,3'-(1,4-phenylene)bis(5-methyl-2-(4-(pyridin-2-	F12

						yl)phenyl)imidazolidin-4-one)	
88	Greenish yellow	0.52	197-199	732.888	C48H40N6O2	3,3'-(1,4-phenylene)bis(5-benzyl-2-(4-(pyridin-2-yl)phenyl)imidazolidin-4-one)	F13
95	yellowish	0.66	216-218	764.886	C48H40N6O4	3,3'-(1,4-phenylene)bis(5-(4-hydroxybenzyl)-2-(4-(pyridin-2-yl)phenyl)imidazolidin-4-one)	F14
99	Greenish yellow	0.61	182-184	552.638	C34H28N6O2	3,3'-(1,4-phenylene)bis(2-(4-(pyridin-2-yl)phenyl)imidazolidin-4-one)	F15
84	brown	0.85	230-232	460.414	C20H16N10O4	,4-bis(5-(4-nitrophenyl)-2,5-dihydro-1H-tetrazol-1-yl)benzene	F16
52	light brown	0.72	236-238	524.592	C30H24N10	1,4-bis(5-(4-(pyridin-2-yl)phenyl)-2,5-dihydro-1H-tetrazol-1-yl)benzene	F17
63	Dark brown	0.61	281-283	522.550	C24H18N4O6S2	3,3'-(1,4-phenylene)bis(2-(4-nitrophenyl)thiazolidin-4-one)	F18
63	Dark brown	0.66	287-289	586.728	C34H26N4O2S2	3,3'-(1,4-phenylene)bis(2-(4-(pyridin-2-yl)phenyl)thiazolidin-4-one)	F19

Results and discussion:

P-phenylenediamine (1 mol) and various aldehydes (2 mol) were reacted in Absolute ethanol to form Schiff bases. The course of the reactions of the prepared compounds was monitored through the use of the thin layer technique, as well as measuring their melting points. The authenticity of the prepared compounds was detected and confirmed through FTIR spectrometry "1H-NMR, and 13C-NMR spectra". FT-IR spectra of Schiff base compounds

(F1-F3) were analyzed using IR Technique and It was observed that the amine group completely disappeared at (3440-3326) cm^{-1} and the appearance of a new azomethine group (C=N) at (1595-1614) cm-1. In the 1H-NMR spectra of the Schiff bases (F1 – F3), a signal peak at 8.57 ppm was caused by a proton of a group (s N = C – H). The spectrum also showed several signals at the same position (6.9-7.9 ppm) that were associated with the aromatic ring's protons in various settings (Ar-H). In Schiff bases' "13C-NMR" spectra, the azomethine imine group appears in the range (155.26-158.41 ppm) from

signal pattern 1 This research uses new derivatives of pentacyclic heterocyclic substances (imidazolidine, tetrazole, and thiazolidine) (F4-F19) were made by the Schiff bases' interaction with (amino acids, thioglycolic acid and sodium azide). The FT-IR spectrum showed Absence of an absorption band associated with the Schiff bases' azomethine group, as well as the amide group (-N-C=O) in the range (1606-1625 cm-1), as well as the appearance of the secondary(N-H) group at the frequency (3188-3419) cm-1, while the compounds were determined using The course of the reactions of the prepared compounds was monitored through the use of the thin layer technique, as well as measuring their melting points. The authenticity of the prepared compounds was detected

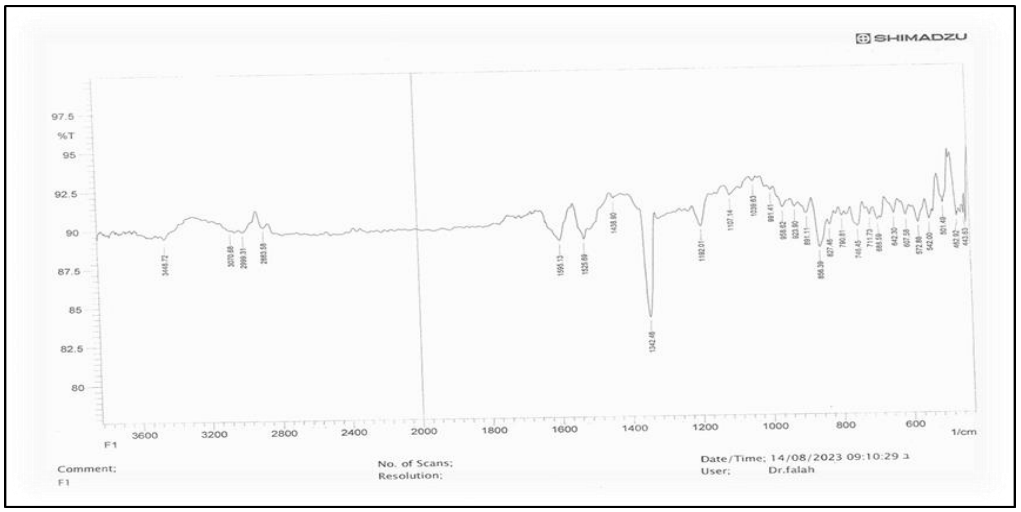


Figure 2 FT-IR Spectrum of compound F1

And confirmed through FTIR spectrometry and. There was a signal at 2.52 ppmbecause of the solvent (DMSO) that was used, and a signal that emerged at (6.09) ppm because of the pentagonal group's protonation (N-CH). Due to the aromatic rings' protonation in various settings, it was found that numerous signals emerge at (6.99-7.90 ppm) (Ar-H), and the proton of the group (-NH-) of the secondary amine appears in the range (9.36-9.67). parts per million). The compounds were also determined by ("13C-NMR") spectra; one signal from the pentameric ring (C-N) occurred in the range of (56.70-71.40 ppm), while a signal from the solvent employed (DMSO) appeared at the site (40 ppm). For (-(CH-NH) in the range (75.56-79.63 ppm), and the signals (112.57-131.52 ppm) which are carbon atoms in the aromatic ring, as well as the appearance of a single signal for the amide group -N-C=O in the range (172.75- 177.79 ppm).

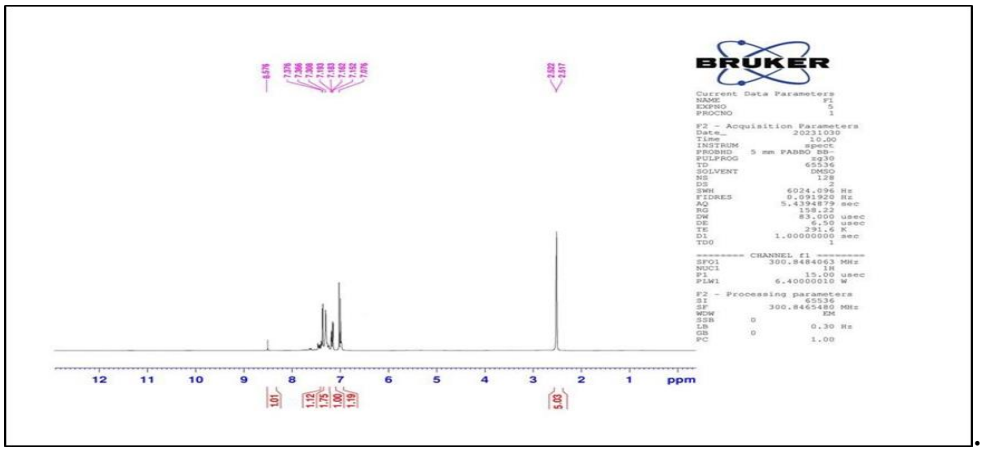


Fig (2)."1H-NMR" Spectrum of The Substance (F1).

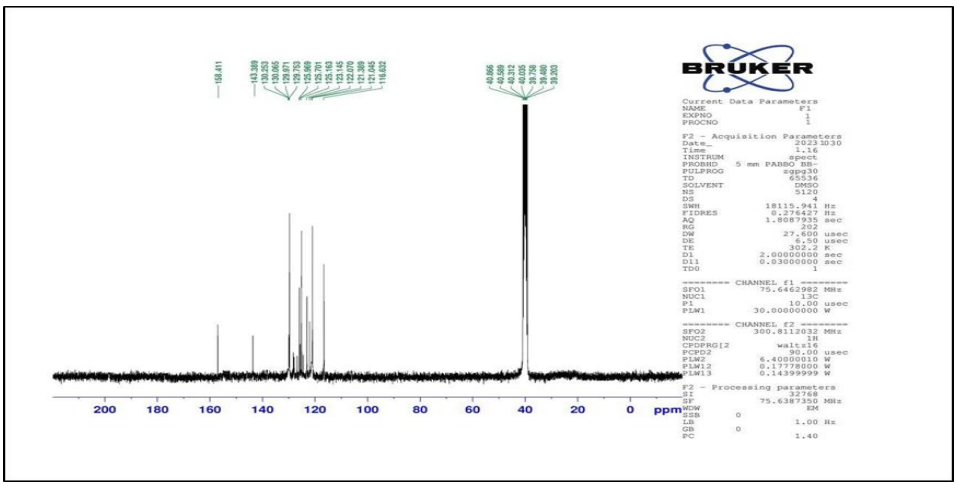


Fig (3): "13C-NMR" Spectrum of the substance (F1)

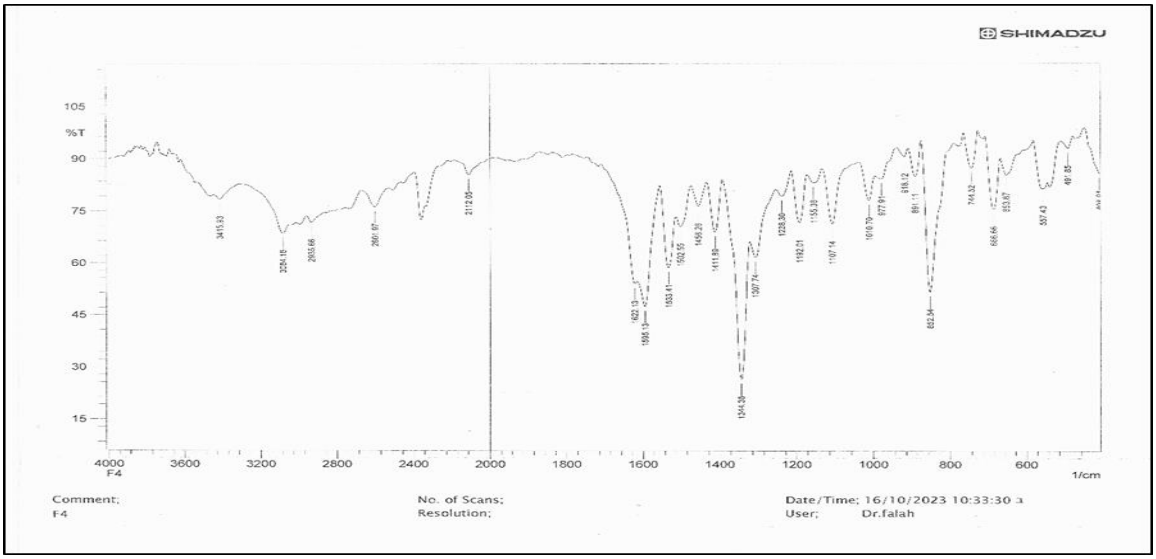


Figure 4 FT-IR Spectrum of compound F4

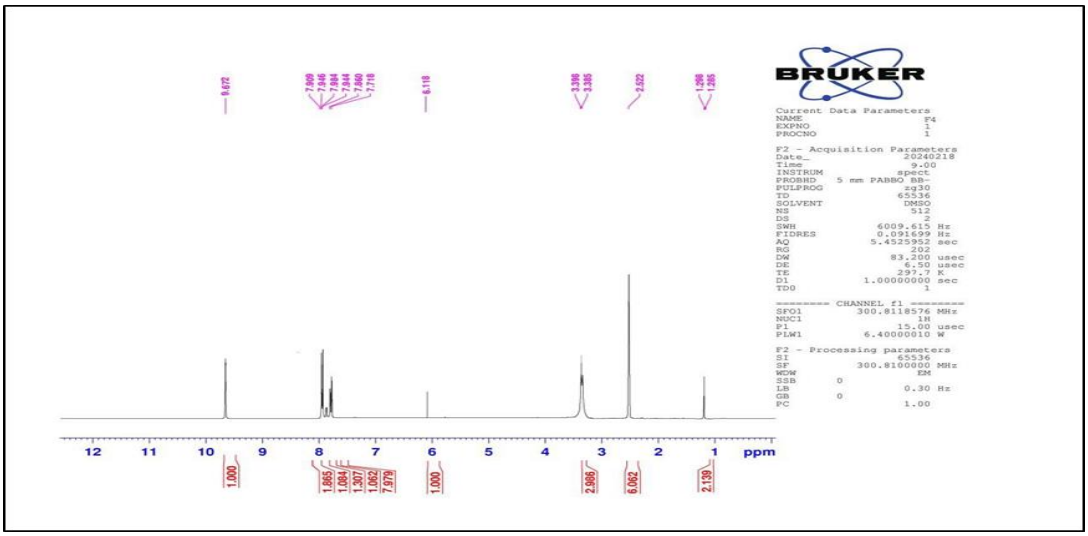


Fig (5):"1H-NMR" Spectrum of the substance (F4)

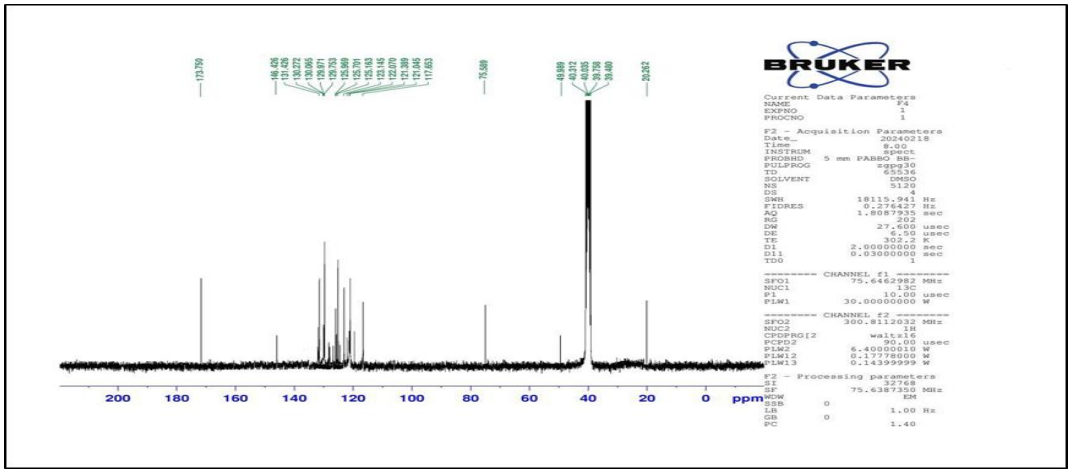


Fig (6):"13C-NMR " Spectrum of the substance (F4)

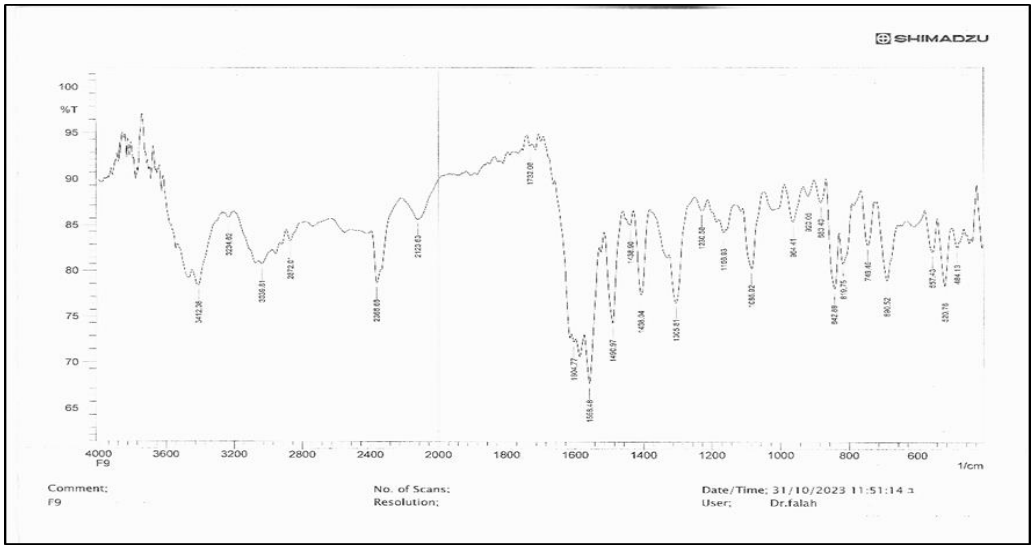


Figure 7 FT-IR Spectrum of compound F9

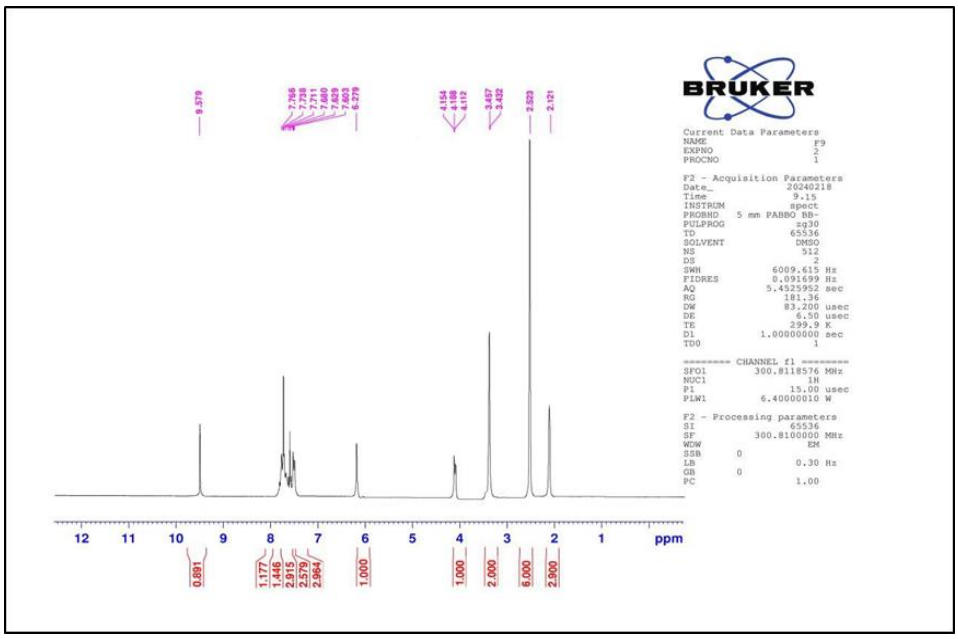


Fig (8): "1H-NMR" Spectrum Of The Substance (F9)

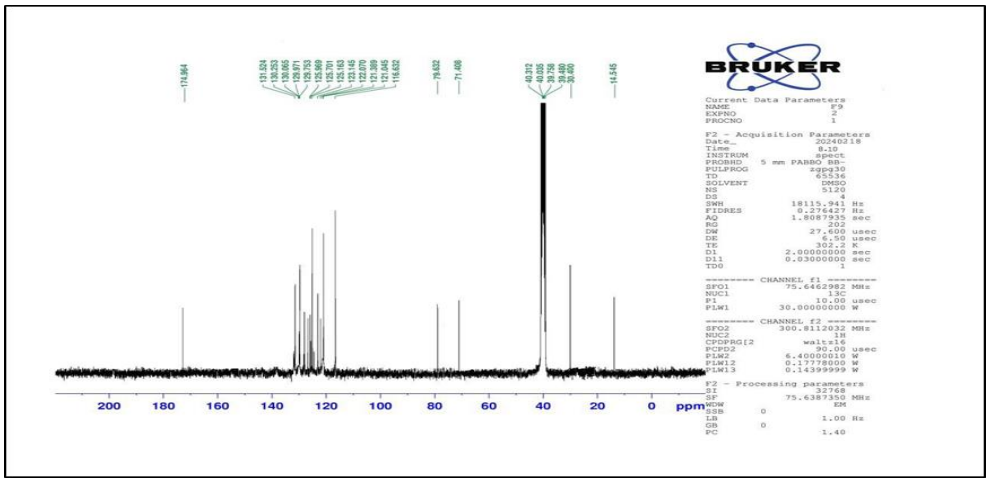


Fig (9):"13C-NMR" Spectrum of the compound (F9)

Biological activity:

Numerous types of bacteria are accountable for most infectious ailments that afflict living organisms, according to research on microorganisms. This has piqued the interest of numerous scientists in developing novel antibiotic compounds that target these bacteria exclusively. This method will be used to investigate the biological activity of two kinds of harmful bacteria that have been isolated: Both Gram-positive (such as *Staphylococcus aureus*) and Gram-negative (such as *Escherichia coli*). When exposed to

the same conditions as the DMSO solvent, the majority of the compounds selected for the biological effects inquiry showed varying degrees of high and medium positive inhibitory findings. A number of the compounds had little to no influence on the development of the bacteria utilized in the experiment because of differences in the binding groups and compounds.

Table (2) shows the effect of the prepared compounds on two types of bacteria

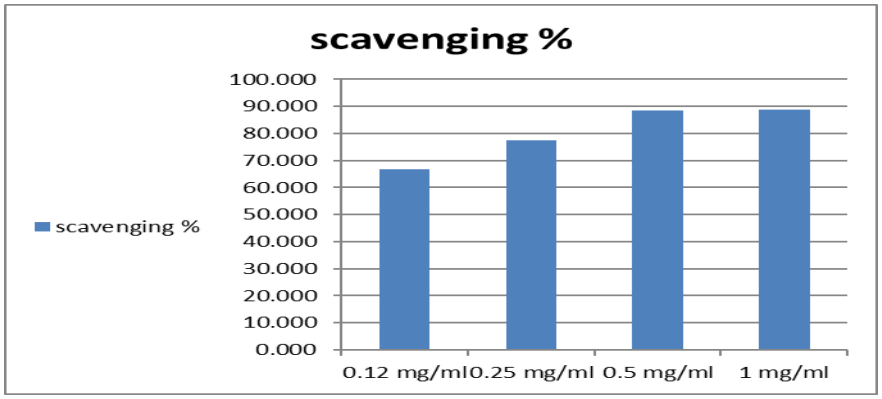
Staph. Aureus	*E. Coli*	Concentration	Material
30	24	0.01 g/ml	F4
21	20		
0.001 g/ml			
28	26	0.01 g/ml	F13
20	15	0.001 g/ml	
29	27	0.01 g/ml	F6

Antioxidant:

Antioxidant analyses' findings demonstrated that, in contrast to ascorbic acid, the active groups of the synthesized compounds—Schiff bases and imidazolidine—had antioxidant qualities. The compounds (F10) demonstrated the highest rate of inhibition when compared to ascorbic acid because they contain groups rich in electrons that can bind with free radicals and prevent oxidation, as shown in table (3). It was discovered that they have a high rate of inhibition at concentrations of 1 mg/ml.

Table (3) shows the antioxidants of the prepared compounds, F10

anti oxidant			
sample name	concentration	absorbency	scavenging %
1	0.12 mg/ ml	0.3342	66.901
2	0.25 mg/ ml	0.2274	77.478
3	0.5 mg/ ml	0.1174	88.373
4	1 mg/ ml	0.1138	88.729



Scheme (3) Anti-oxidants for(F3) compounds

Study of molecular docking.

The aforementioned data make it abundantly evident that the chemical F2, which was selected as a means of treating Escherichia coli germs, gave the lowest binding energy of all the protein types (2q85). It was found that compound F2 and compound 10 gave the lowest binding energies in the bacteria (Staph. aureus), while compound F10 gave the lowest binding energy. Compound F2 has a potential therapeutic potential with protein (2q85), while compound F10 has a potential therapeutic potential with protein (2xct).

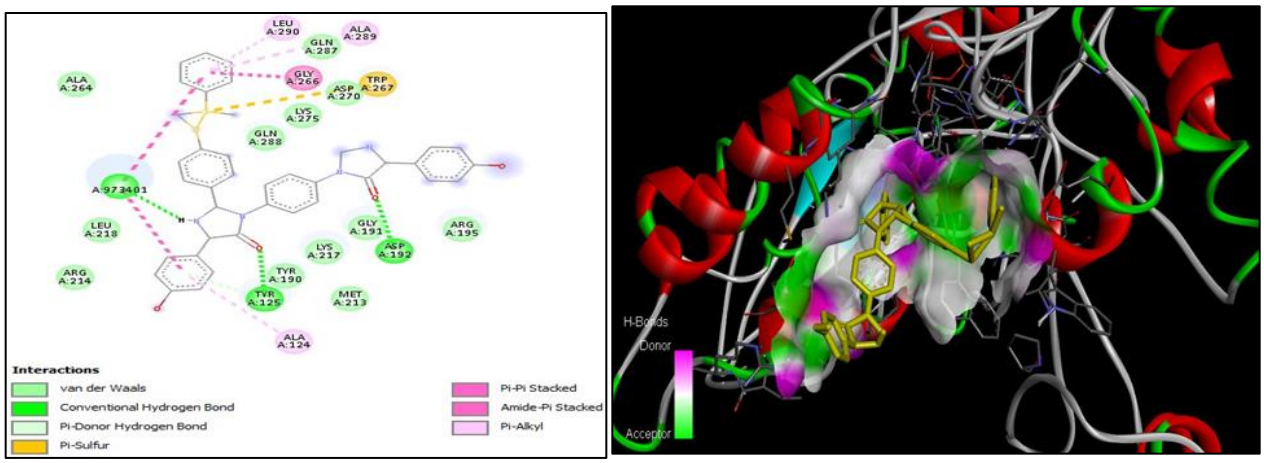


Figure 10 2D & 3D interaction diagrams representing the docked conformation of ligand F10 against 2xct

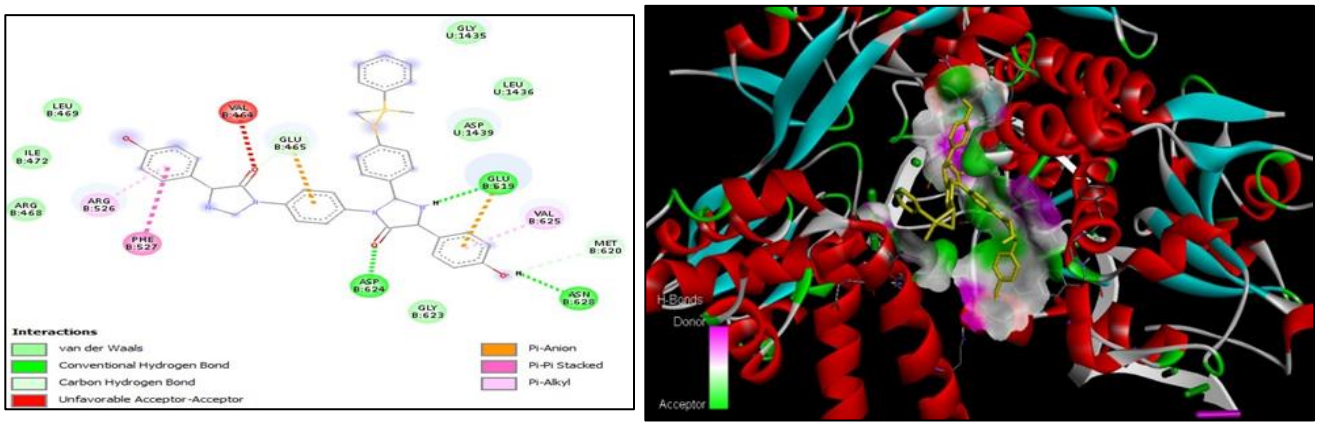


Figure 3.82 2D & 3D interaction diagrams representing the docked conformation of ligand F10 against 2q85

Composite F10 Results of molecular conjunction between compounds and bacteria (*E. coli*) Protein is (2q85)

Compound NO.	Lowest Binding Energy	Run
F10	-7.88	18

Composite F10 Results of molecular conjunction between compounds and bacteria (*Staph. Aureus*) Protein is (2xct)

Compound NO.	Lowest Binding Energy	Run
F10	**-9.94**	**36**

Proposed Structural:

In conclusion, a method was found to synthesize Schiff bases using two moles of different aldehydes with one mole of *p*-phenylenediamine, then reacting the products (Schiff bases) by taking one mole of them with two moles of (different amino acids, sodium azide and thioglycolic acid) To produce new heterogeneous rings. Five rings. (Imidazolidine, thiazolidine and tetrazole) in absolute ethanol Based on "FT-IR, 1H-NMR" and "13C-NMR spectroscopic "data, the structures of all heterocyclic derivatives synthesized in this study were established.

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