SYNTHESIS, IDENTIFICATION OF SOME NEW TETRAZOLINE, THIAZOLIDIN-4-ONE AND IMIDAZOLIDIN-4-ONE DERIVATIVES AND EVALUATION ANTICANCER OF THEIR MOLECULAR DOCKING AND ANTI-OXIDANT EXPERIMENTAL

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ABSTRACT

In this study, a new series of 1,3-dimethyl-6-(amino aceto hydrazine) pyrimidine-2,4-dione-6-yl with 4-substituted benzyldehyde, The compound (1-5) was synthesized in a single pot that cyclization by the addition of sodium azide, 2-mercapto acid & 2-amino acetic acid to produce five-membered heterocyclic rings includes: tetrazoline-1yl (6-10), thiazolidin-4-one (11-15) and imidazolidin-4-one (16-20) derivatives respectively. These compounds were characterized using spectral methods [FTIR and 1HNMR, 13C-NMR for some of them] evaluations, measurements, and analyses of their physical qualities. Each molecule was evaluated for antioxidant activity in vitro to use the DPPH and phosphomolybdenum methods. When compared to the standard drug Ascorbic acid, (1-20) demonstrated promising antioxidant activity among the bioactive molecules synthesized. Furthermore, molecular docking against, substances showed superiority over the standard medication Exemestane in tests of the Aromatase enzyme.

KEYWORDS

Tetrazoline, Thiazolidin-4-one, Imidazolidin-4-one, molecular docking and Anti-oxidant

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1. INTRODUCTION

Uracil is an essential pyrimidine representative. It is one of the five nucleobases and a promising structure in many natural products [1]. Uracil derivatives are important intermediates in the purine synthesis. One of the four nucleobases that make up RNA, it is a pyrimidine derivative that occurs naturally. In RNA, uracil couples to adenine via two hydrogen bonds. DNA with thymine instead of uracil [2, 3].

Compounds containing a high nitrogen content constitute a distinct class of C-N heteroaromatic compounds [4]. The tetrazoline ring structure contains unsaturated bonds, which ensures good energy properties [5]. Due to its high nitrogen concentration, enthalpy of formation [6], and inclination toward lesser sensitivity, tetrazoline is commonly employed in the construction of high-energy density materials [7].

Thiazolidinone derivatives have a five-membered heterocyclic ring with one sulfur, one nitrogen, and three carbon atoms Thiazolidinones are one of the most essential heterocyclic compounds [8], and their derivatives, which have a carbonyl group in the fourth position, are an integral part of many synthetic pharmaceuticals with diverse biological activities [9, 10]

4-Imidazolidinones are a class of nitrogen-rich saturated lactams with medicinal applications [11]. Imidazolidinone derivatives are currently of interest as organocatalysts in modern organic synthesis [12]. 4-Imidazolidinones are cyclic amides, whereas 2-Imidazolidinones are cyclic urea compounds. illustrates imidazolidinone isomers [13]. The imidazolidin-2-one motif is frequently found in natural products1,2 as well as pharmaceutically interesting synthetic molecules [14].

as a result of their ease of synthesis, uracil derivatives are regarded as promising compounds in drug discovery. The pyrimidine core is an important pharmacophore moiety of biologically active natural and synthetic compounds that compete for the same binding sites[15] the most conmen biological activities of uracil derivatives in the last years application Antioxidan t[2], Anti-flamatory [16], Anticaner [17], Anti-leukemia [18], Antibacterial [19, 20], anti-tumour [21], anti-angiogenesis [22] and Anti-diabetic [23].

2. MATERIALS AND METHODS

The investigation relied on unpurified chemicals purchased from BDH, Fluka, Merck, and Sigma Aldrich. In addition, an Electro thermal melting point device was used to record the melting points, although no corrections were made. Using a SHIMAZU FTIR-8400 Fourier transform Infrared spectrophotometer, KBr discs were used to record the (4000-600) cm-1 FTIR spectra of the produced compounds. Using a BRUKER 400MHz equipment, TMS was used as the internal standard, and DMSO-d6 was used as the solvent in order to get 1H- and 13C-NMR spectra in Iraq. The Adiwaniyah Technical Institute and the Al-Forat Alawsat University both employed Japanese Shimadzu 1900i spectrophotometers.

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2.1. SYNTHESIS OF 1,3-DIMETHYL-6- (AMINO ACETO HYDRAZIDE BENZYLIDENE)- PYRAMIDINE-2, 4-DIONE-6-YL.(1-5)[24, 25]

A solution of (0.5 g, 0.022 mol.) 1,3-dimethyl-6-(amino aceto hydrazine) pyrimidine-2,4-dione-6-yl, (0.022 mol.) para substituted aromatic aldehydes in (10 mL) of ethanol absolute as a solvent were thoroughly mixed with glacial acetic acid as a catalytic three drops of, and the mixture was refluxed for (6-10) house. The product was filtrated, water washed and recrystallized by ethanol Table-2 lists characteristics of compounds in terms of their physical properties (6-10) as well as FTIR spectral data.

2.2. SYNTHESIS OF 1,3-DIMETHYL-6-AMINO ACETAMIDE[5-(4-SUBSTITUTED PHENYL)-2H-TETRAZOLINE-1-YL]-PYRAMIDINE-2,4-DIONE-6-YL.(6-10) [26, 27]

Compounds (6-10) were obtained from reaction of an equimolar a combination of Schiff bases (1-5) (0.0009 mol.) in ethanol (10 mL). Sodium azide (0.05 g, 0.0009 mol.) dissolved in the same solvent was added and the solution was reflex for (18-20) house. The product was filtrated, water washed and recrystallized by ethanol Table-2 lists some of the physical properties of compounds (6-10) as well as FTIR spectral data.

2.3. SYNTHESIS OF 1,3-DIMETHYL-6-AMINO ACETAMIDE[2-(4-SUBSTITUTED PHENYL)-THIAZOLIDIN-4-ONE-3-YL]-PYRAMIDINE-2,4-DIONE-6-YL.(11-15)[28]

Throughout this step, (0.0009 mol.) of compound (1-5) of Schiff bases and (0.06 mL., 0.0009 mol.) of 2-mercaptoacetic acid were added dropwise to THF (10 mL). After that, the reaction mixture was heated to reflux temperature (20-24). The mixture was filtered, washed, and purified further with ethanol to recrystallization. Table-3 contains a list of a variety of physical properties of compounds (11-15) as well as FTIR spectral data.

2.4. SYNTHESIS OF 1,3-DIMETHYL-6-AMINO ACETAMIDE[2-(4-SUBSTITUTED PHENYL)-IMIDAZOLIDINE-4-ONE-3-YL]-PYRAMIDINE-2,4-DIONE-6-YL.(16-20)[29, 30]

An equimolar amount of Schiff bases (1-5) is added to a mixture (0.0009 mol.) As a solvent, (10 mL) of ethanol was stirred in, with (0.25 g, 0.0009 mol.) 2-aminoacetic acid in the same solvent and the mixture solution was refluxed for (20-22) house. The resulting mix was then result of filtering being reformed from acetone crystals after being allowed to cool to room temperature. Table-3 lists a variety of physical properties of compounds (16-20) as well as FTIR spectral data.

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Table 1. the physical properties as well as the FTIR spectral data cm-1 of the compounds that were produced (1-5).

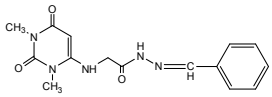
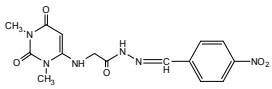
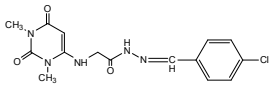
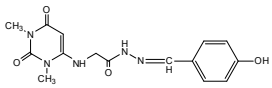
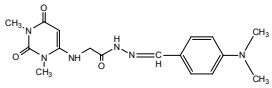
Com. No.	Physical properties				Major FTIR Absorptions cm^{-1}				
	Compound Structure	m.p °C	Yield %	Color	νN-H	νC-H Arom. Aliph.	ν(C=O)	ν(C=N) ν(C=C)	Other bands
1		88-90	80	Pale gray	3282	3053 2952	1701 1681	1639 1623	-
2		222-223	85	yellow	3294	3001 2975	1701 1683	1639 1620	(NO2) Asym. 1521 Sym. 1346
3		187-188	77	Light gray	3294	3099 2997 2943	1731 1683	1649 1625	(C-Cl) 1091
4		268-270	70	Light yellow	3301	3028 2960	1730 1656	1627 1619	ν(-OH) 3433
5		250-251	85	Reddish yellow	3292	3060 2979	1699 1681	1639 1620	-

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Table 2. the physical properties as well as the FTIR spectral data cm-1 of the compounds that were produced (6-10).

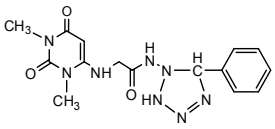
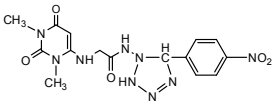
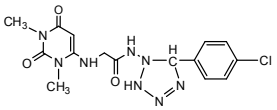
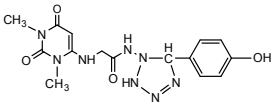
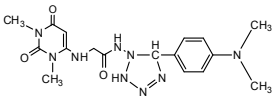
Com. No.	Physical properties				Major FTIR Absorptions cm^{-1}				
	Compound Structure	m.p °C	Yield %	Color	νN-H	νC-H Arom. Aliph.	ν(C=O)	ν(C=C)	Other bands
6		359-360	80	Deep yellow	3275	3023 2923	1708 1668	1620	ν(N=N) 1450
7		310-311	77	Light yellow	3290	3024 2975	1703 1687	1622	ν(N=N) 1451 ν(NO2) Asym. 1523 Sym. 1346
8		359-360	75	Yellow	3286	3077 2997	1711 1685	1625	ν(C-Cl) 1089 ν(N=N) 1453
9		260-261	84	Deep gray	3319	3028 2958	1710 1682	1608	ν(N=N) 1448 ν(-OH) 3406
10		268-269	83	Yellow	3282	3050 2962	1703 1685	1625	ν(N=N) 1457

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Table 3. the physical properties as well as the FTIR spectral data cm-1 of the compounds that were produced (11-15).

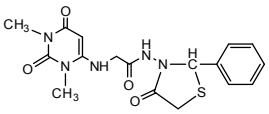
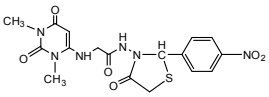
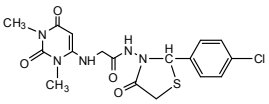
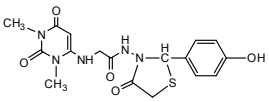
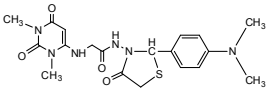
Com. No.	Physical properties				Major FTIR Absorptions cm^{-1}				
	Compound Structure	m.p °C	Yield %	Color	νN-H	νC-H Arom. Aliph.	ν(C=O)	ν(C=C)	Other bands
11		270-271	81	Light yellow	3350	3060 2956	1699 1674	1620	ν(C-S) 709
12		302-303	84	Yellow	3382	3002 2974	1701 1685	1618	ν(NO2) Asym. 1521 Sym. 1346 ν(C-S) 702
13		212-213	78	Deep gray	3286	3097 2983	1733 1683	1625	ν(C-Cl) 1091 ν(C-S) 700
14		230-231	79	Deep gray	3269 3253	3060 2974	1701 1683	1626	ν(-OH) 3444 ν(C-S) 703
15		264-265	82	Yellow	3284	3060 2981	1701 1685	1628	ν(C-S) 696

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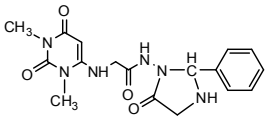
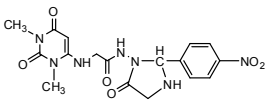
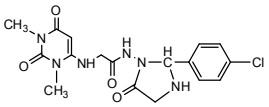
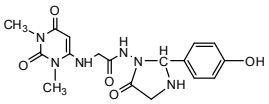
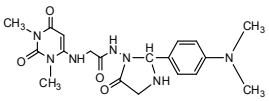
Table 4. the physical properties as well as the FTIR spectral data cm-1 of the compounds that were produced (16-20).

Com. No.	Physical properties				Major FTIR Absorptions cm^{-1}				
	Compound Structure	m.p °C	Yield %	Color	νN-H	νC-H Arom. Aliph.	ν(C=O)	ν(C=C)	Other bands
16		253-254	81	Yellow	3180	3051 2977	1731 1666	1612	-
17		270-271	86	Deep yellow	3211	3050 2958	1693 1672	1630	ν(NO2) Asym. 1521 Sym. 1344
18		193-194	79	Deep gray	3180	3049 2995	1713 1662	1622	ν(C-Cl) 1089
19		224-225	75	Reddish yellow	3180	3062 2987	1692 1662	1610	ν(-OH) 3413
20		262-263	82	Light yellow	3298	3060 2977	1701 1683	1625	-

2.5. ACTIVATION OF ANTIOXIDANT DEFENSES (DPPH RADICAL SCAVENGING ASSAY)[31, 32]

Activation of antioxidant defenses was measured for a range of compounds (1-20) using a conventional method and the stable DPPH free radical. The compounds 1–20 were produced in DMSO at three different concentrations (50, 100, and 150) M, after which it was put to a methanol solution (of up to 2 milliliters) that contained 0.0002 grams per milliliter of DPPH radical. After 30 minutes of room temperature incubation, the spectrophotometer was utilized for determining the absorbance of the reaction mixture at a wavelength of 517 nm. Ascorbic acid served as a reference substance when evaluated at the same quantities as the other substances. To determine how effective ascorbic acid was in blocking DPPH radicals, we used the following formula: ((Ac-As)/Ac) *100. (percentage). An absorbance measurement taken from a control (Ac) and one taken from a sample (As) are shown.

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2.6. TOTAL ANTIOXIDANT CAPACITY[33]

It was revealed that the compounds that were synthesized had a total antioxidant capability when they were tested with the phosphomolybdenum technique. An aliquot of a solution containing the chemical was combined with one milliliter of reagent that included 0.6 M sulphuric acid, 28 mM (Na2HPO4), and those were all included (4 mM ammonium molybdate). After that, a hermetic seal was placed on each of the test tubes that contained the reaction solution for the compounds that were being analyzed, and the tubes were then heated to 95 degrees Celsius for an hour and a half. After bringing the temperature in the room up to room temperature, a spectrophotometer was used to measure the absorbance of each tube at 695 nm in comparison to a blank. The total antioxidant activity is reported as the amount of ascorbic acid that is comparable to one gram. For the purpose of plotting the calibration curve, the following concentrations of ascorbic acid in DW were used: 10, 20, 30, 50, 70, 90, 120, 180, and 200 g/mL.

2.7. IN SILICO STUDIES

2.7.1. PREPARATION OF THE LIGAND[2]

Molecular docking research was carried out making use of the Small Drug Research Suites software package (Schrodinger 2020-3, LLC). The two-dimensional it was decided to draw out the structures of the freshly produced substances, and then Maestro 12.5 was used to turn those drawings into three-dimensional structures. Before docking, the ligands' pH levels were brought up to the physiological range using the OPLS2005 force field, and energy was reduced as much as possible. The Epik choice was made so that the ligand could remain in the correct protonation state throughout the process.

2.7.2. DETERMINING PROTEIN BINDING REGIONS

We uploaded the three-dimensional crystal structure of the aromatase enzyme, which may be found in the RCSB Protein Data Bank (PDB ID: 3S7S). The 3D crystal structure has been fixed and prepared with the help of Maestro 12.5's protein preparation wizard. To get started, the crystal structure had every last trace of water vapor evaporated. The protein's bond orders and charges were determined before any of the missing hydrogen atoms were added. Ionization of amino acids was achieved through adjustment of the physiological pH via the Propka software. As a final step, the OPLC force field was used for restrained minimization. For docking purposes, this streamlined structure worked wonderfully. After protein preparation, the best protein binding site was determined by identifying the highest-ranked potential protein binding sites utilizing the use of the maestro 12.5 glide grid program.

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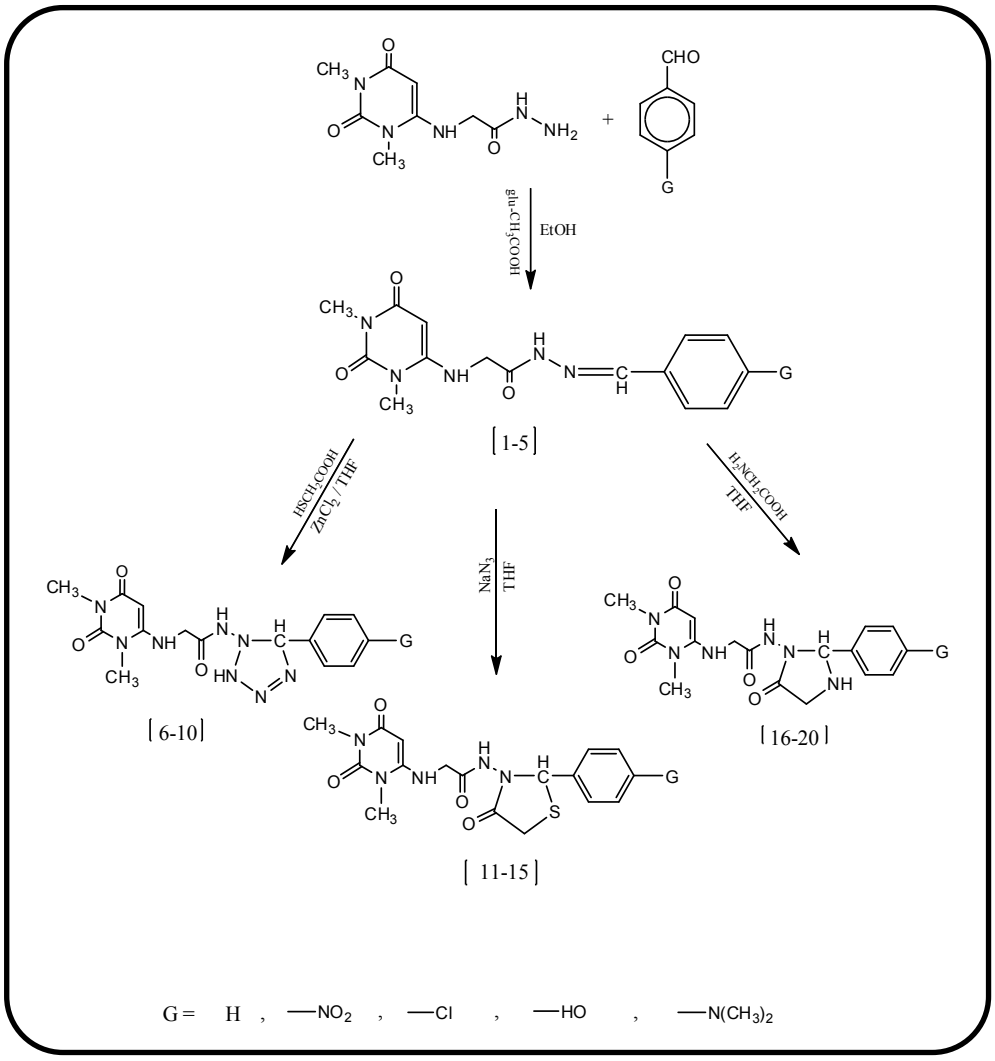
2.7.3. MOLECULAR DOCKING INVESTIGATION

Binding sites on the receptor were located using the glide grid tool, and the best ligand poses and binding energies were predicted using ligand docking. To begin, the Glide docking module in Maestro 12.5 was used to successfully dock all ligands onto their corresponding receptors. A grid box was generated using the receptor grid generation platform in the region of the co-crystallized ligand that is favored at the binding site. Maestro 12.5 was used to perform the simulations. Last but not least, the maestro 12.5 work space visualizer was used to visualize poses and analyze the resulting data.

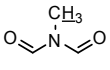
3. RESULTS AND DISCUSSION

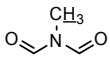
Synthetisesed Using Schiff bases of 1,3-dimethyl-6-(amino aceto hydrazine) pyrimidine-2,4-dione-6-yl and various reagents, a series of new heterocyclic rings with five members was synthesized Scheme-1. This series includes tetrazoline, thiazolidin-4-one and imidazolidine-4-one.



https://doi.org/10.17993/3ctic.2023.121.83-116

3.1. SCHEME-1 SYNTHESIS OF NEW TETRAZOLINE, THIAZOLIDIN-4-ONE, AND IMIDAZOLIDINE-4-ONE DERIVATIVES

The first step in the synthesis of new in Scheme-1 tetrazol, thiazolidin-4-one, and imidazolidine-4-one derivatives. A solution of 1,3-dimethyl-6-(amino aceto hydrazine) pyrimidine-2,4-dione-6-yl, para substituted aromatic aldehydes and absolute ethanol Its solvents were thoroughly combined with glacial acetic acid a catalytic three drops to synthesized Schiff bases derivatives (1-5) in table-1 showed the physical properties and FTIR of compound (1-5). The FTIR spectrum[34] showing in figure(1-5) includes the presence of a v(N-H) at (3301-3282) cm^{-1}; v(C-H) Arom. at (3099-3001) cm^{-1}; v(C-H) Aliph. at (2997-2941) cm^{-1}; v(C=O) at (1731-1656) cm^{-1}, v(C=N) at (1649-1627) cm^{-1} and v(C=C) at (1625-1619) cm^{-1} of compound (1-5). The compound (2) have v(-NO_2) in asym. at (1521 cm^{-1}) and sym. at (1346 cm^{-1}); compound (3) have v(C-Cl) at (1091 cm^{-1}) and compound (4) have v(-OH) at (3433 cm^{-1}). Compound (5) ^{1}H-NMR spectra data, all signals shown in table-5 and showing in Figure 21 that contain signal 2.51 (s, 6H, N-(C**H**$_3$)$_2$); 2.96 (s, 3H, N-C**H**$_3$); 2.99 (s, 3H, ); 3.4 (s, 1H, N**H**); 3.51 (s, 2H, C**H**$_2$); 3.57 (s, 1H, =C**H**); 6.75 (s, 1H, N=C-**H**); 7.63-8.49 (m, 4H, Ar-**H**); 9.66 (s, 1H, **H**N-N). Table-6 shows the ^{13}C-NMR spectrum data of this compound (5) and showing in Figure 22.

Synthisesed compounds (6-10) by cyclization compound (1-5) through sodium azide in ethanol as solvent as showing in scheme-1. In table-2 showed the physical properties and FTIR of compound (6-10). The FTIR spectrum of tetrazoline derivatives showing in figure(6-10) includes the presence of a v(N-H) at (3319-3275) cm^{-1}; v(C-H) Arom. at (3077-3023) cm^{-1}; v(C-H) Aliph. at (2997-2923) cm^{-1}; v(C=O) at (1711-1668) cm^{-1}, v(C=C) at (1625-1608) cm^{-1} and v(N=N) at (1457-1448) $cm^{-1}$of compound (6-10). The compound (7) have v(-NO_2) in asym. at (1523 cm^{-1}) and sym. at (1346 cm^{-1}); compound (8) have v(C-Cl) at (1089 cm^{-1}) and compound (10) have v(-OH) at (3406 cm^{-1}). Compound (7) ^{1}H-NMR spectra data, all signals shown in table-5 and showing in Figure 23 that contain signal at 2.5 (s, 3H, N-C**H**$_3$); 2.5 (s, 3H, ); 3.45 (s, 2H, C**H**$_2$); 3.46 (s, 1H, N**H**); 3.56 (s, 1H, N-C**H** tetrazoline ring); 3.62 (s, 1H, =C**H**); 4.9 (s, 1H, N-N**H**-N); 7.5-8.3 (m, 4H, Ar-**H**); 9.5 (s, 1H, **H**N-N).

Compounds (11-15) were synthesized by cyclizing compounds (1-5) through 2-mercaptoacetic in THF as the solvent, as in Scheme-1. In table-3 showed the physical properties and FTIR of compound (11-15). The FTIR spectrum of Thiazolidin-4-one derivatives showing in figure(11-15) includes the presence of a v(N-H) at (3350-3253) cm^{-1}; v(C-H) Arom. at (3097-3002) cm^{-1}; v(C-H) Aliph. at (2983-2956) cm^{-1}; v(C=O) at (1733-1683) cm^{-1}, v(C=C) at (1628-1618) cm^{-1} and v(C-S) at (709-696) $cm^{-1}$of compound (11-15). The compound (12) have v(-NO_2) in asym.

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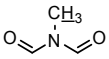
at (1521 cm^{-1}) and sym. at (1346 cm^{-1}); compound (13) have v(C-Cl) at (1091 cm^{-1}) and compound (14) have v(-OH) at (3444 cm^{-1}). Compound (13) ^{1}H-NMR spectra data, all signals shown in table-5 and showing in Figure 24 that contain signal 2.5 (s, 3H, N-C**H**$_3$); 2.5 (s, 3H, ); 3.58 (s, 2H, C**H**$_2$); 3.83 (s, 2H, S-C**H**$_2$); 3.98 (s, 1H, N**H**); 4.1 (s, 1H, N-C**H** thiazolidinone ring); 4.2 (s, 1H, =C**H**); 7.5-8.3 (m, 4H, Ar-**H**); 8.7 (s, 1H, **H**N-N). Table-6 shows the ^{13}C-NMR spectrum data of this compound (13) and showing in Figure 25.

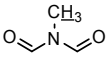
Synthisesed compound (16-20) by cyclization compound (1-5) through glycine in ethanol as solvent as in scheme-1. In table-4 showed the physical properties and FTIR of compound (16-20). The FTIR spectrum of imidazolidine-4-one derivatives showing in figure(16-20) includes the presence of a v(N-H) at (3298-3180) cm^{-1}; v(C-H) Arom. at (3062-3049) cm^{-1}; v(C-H) Aliph. at (2995-2958) cm^{-1}; v(C=O) at (1731-1662) cm^{-1} and v(C=C) at (1630-1610) cm^{-1} of compound (16-20). The compound (17) have v(-NO_2) in asym. at (1521 cm^{-1}) and sym. at (1344 cm^{-1}); compound (18) have v(C-Cl) at (1089 cm^{-1}) and compound (19) have v(-OH) at (3413 cm^{-1}). Compound (16) ^{1}H-NMR spectra data, all signals shown in table-5 and showing in Figure 26 that contain signal 2.5 (s, 3H, N-C**H**$_3$); 2.5 (s, 3H, ); 3.17 (s, 2H, C**H**$_2$); 3.17 (s, 2H, C**H**$_2$-NH); 3.38 (s, 1H, N**H**); 3.57 (s, 1H, N-C**H** imidazolidinone ring); 3.59 (s, 2H, N-C**H**$_2$); 3.64 (s, 1H, =C**H**); 7.5-8.3 (m, 4H, Ar-**H**); 8.7 (s, 1H, **H**N-N).

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Table 5. 1H-NMR of compound (5, 7, 13 and 16)

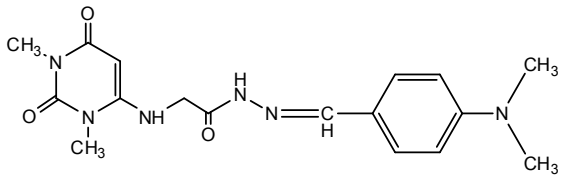
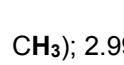
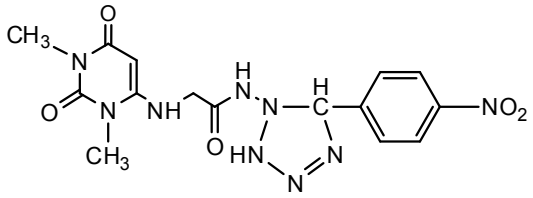
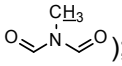
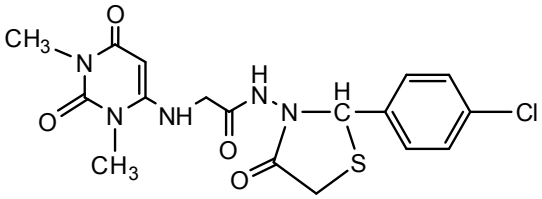
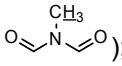
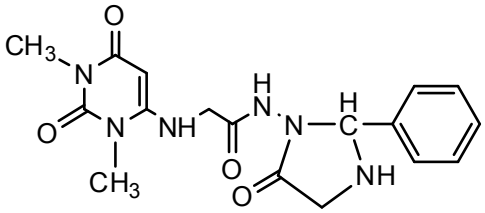
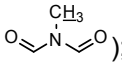
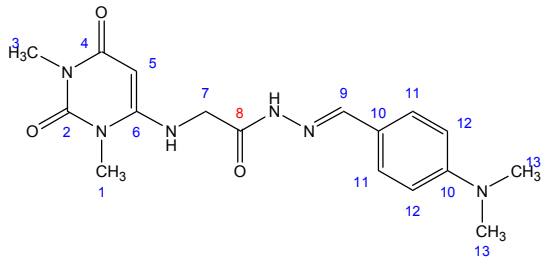
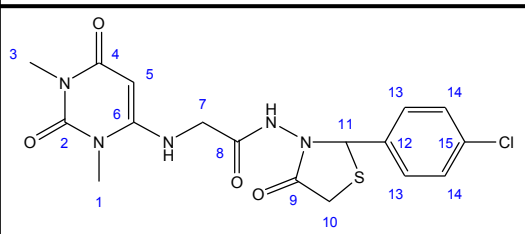
No.	Compound structure	^{1}H-NMR spectral data (δppm)
5		2.51 (s, 6H, N-(C**H**$_3$)$_2$); 2.96 (s, 3H, N-C**H**$_3$); 2.99 (s, 3H, ); 3.4 (s, 1H, N**H**); 3.51 (s, 2H, C**H**$_2$); 3.57 (s, 1H, =C**H**); 6.75 (s, 1H, N=C-**H**); 7.63-8.49 (m, 4H, Ar-**H**); 9.66 (s, 1H, **H**N-N)
7		2.5 (s, 3H, N-C**H**$_3$); 2.5 (s, 3H, ); 3.45 (s, 2H, C**H**$_2$); 3.46 (s, 1H, N**H**); 3.56 (s, 1H, N-C**H** tetrazoline ring); 3.62 (s, 1H, =C**H**); 4.9 (s, 1H, N-N**H**-N); 7.6-8.4 (m, 4H, Ar-**H**); 9.5 (s, 1H, **H**N-N)
13		2.5 (s, 3H, N-C**H**$_3$); 2.5 (s, 3H, ); 3.58 (s, 2H, C**H**$_2$); 3.83 (s, 2H, S-C**H**$_2$); 3.98 (s, 1H, N**H**); 4.1 (s, 1H, N-C**H** thiazolidinone ring); 4.2 (s, 1H, =C**H**); 7.5-8.2 (m, 4H, Ar-**H**); 8.7 (s, 1H, **H**N-N)
16		2.5 (s, 3H, N-C**H**$_3$); 2.5 (s, 3H, ); 3.17 (s, 2H, C**H**$_2$); 3.17 (s, 2H, C**H**$_2$-NH); 3.38 (s, 1H, N**H**); 3.57 (s, 1H, N-C**H** imidazolidinone ring); 3.59 (s, 2H, N-C**H**$_2$); 3.67 (s, 1H, =C**H**); 7.5-8.3 (m, 4H, Ar-**H**); 8.7 (s, 1H, **H**N-N)

Table 6. 13C-NMR of compound (5 and 13)

No.	Compound structure	^{13}C-NMR spectral data (δppm)
5		28.31 (**C**$_1$, **C**$_3$); 58.23 (**C**$_7$); 65.03 (**C**$_5$); 111.23 (**C**$_{11}$); 112.35 (**C**$_{12}$); 129.97 (**C**$_{10}$); 152.54 (**C**$_6$, **C**$_9$); 160.31 (**C**$_2$, **C**$_4$); 165.14 (**C**$_8$)
13		28.31 (**C**$_1$, **C**$_3$); 38.23 (**C**$_{10}$); 59.11 (**C**$_7$); 61.13 (**C**$_{11}$); 66.01 (**C**$_5$); 129.18 (**C**$_{13}$); 133.05 (**C**$_{14}$); 136.17 (**C**$_{12}$); 138.26 (**C**$_{15}$); 152.12 (**C**$_6$); 160.06 (**C**$_2$, **C**$_4$); 166.93 (**C**$_8$, **C**$_9$)

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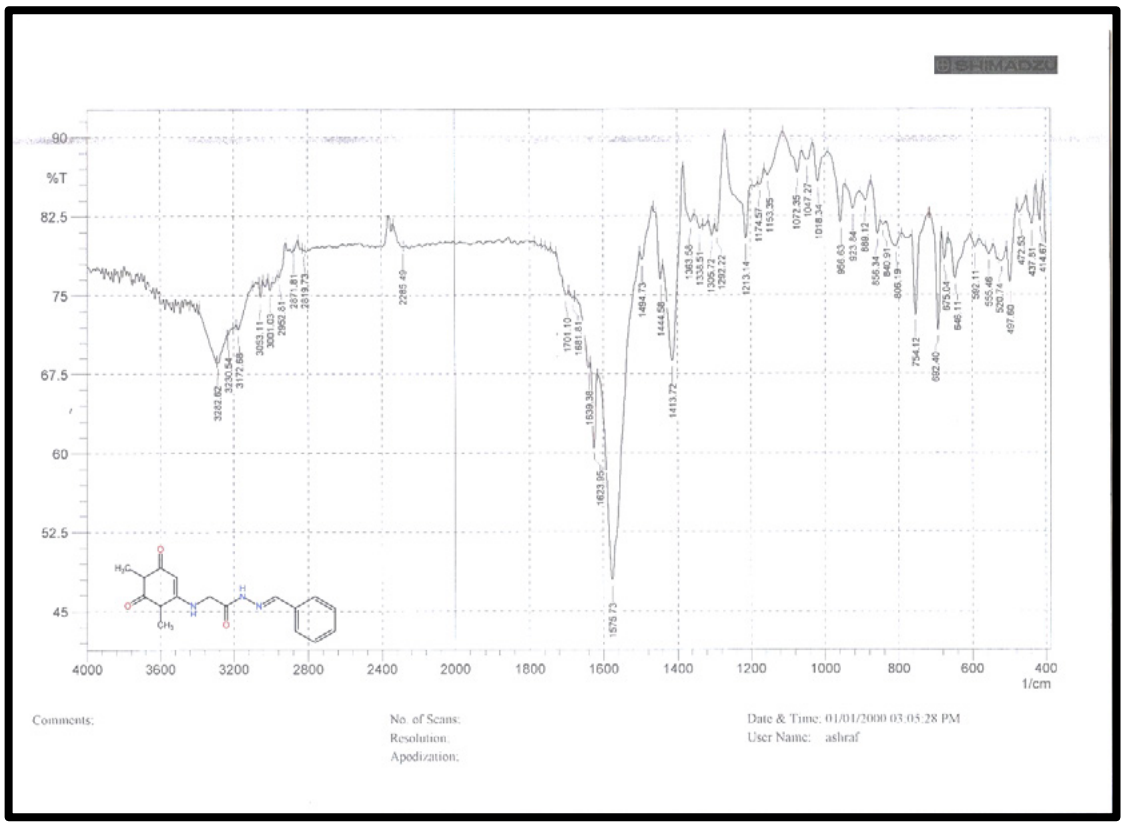

Figure 1. FTIR Soectrum of Compound (1)

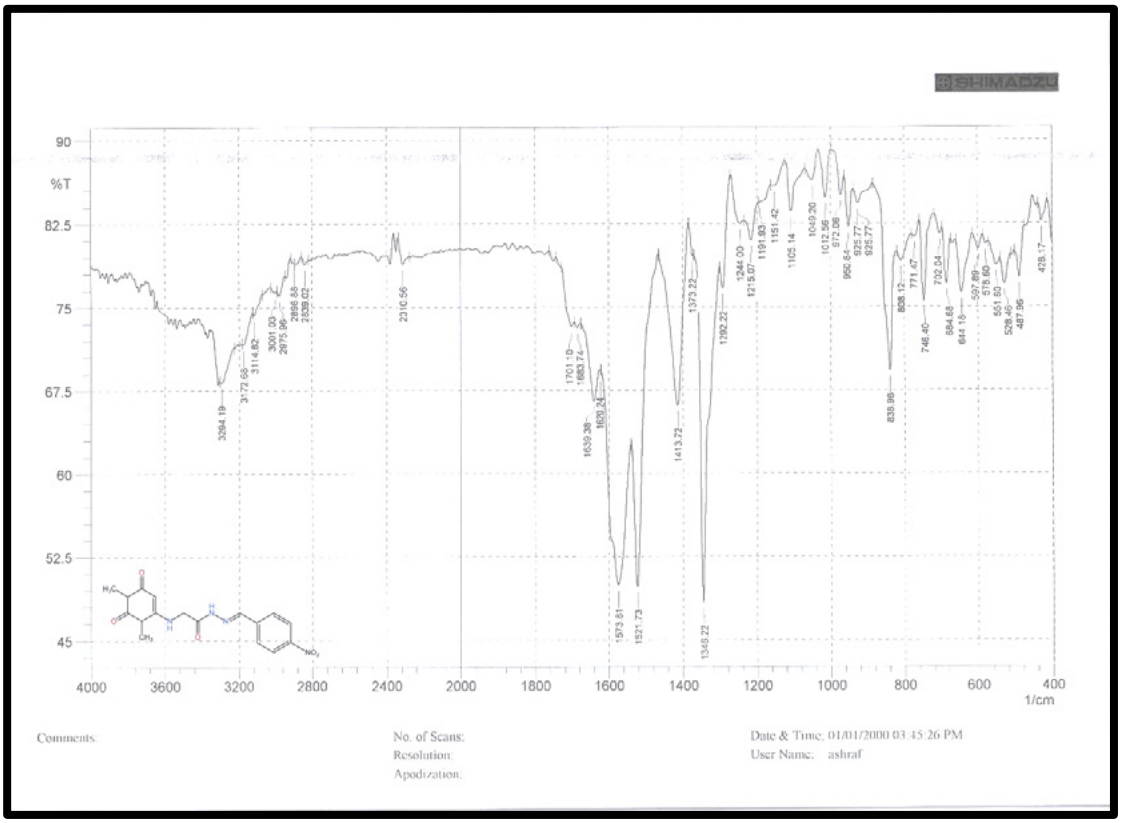

Figure 2. FTIR Soectrum of Compound (2)

https://doi.org/10.17993/3ctic.2023.121.83-116

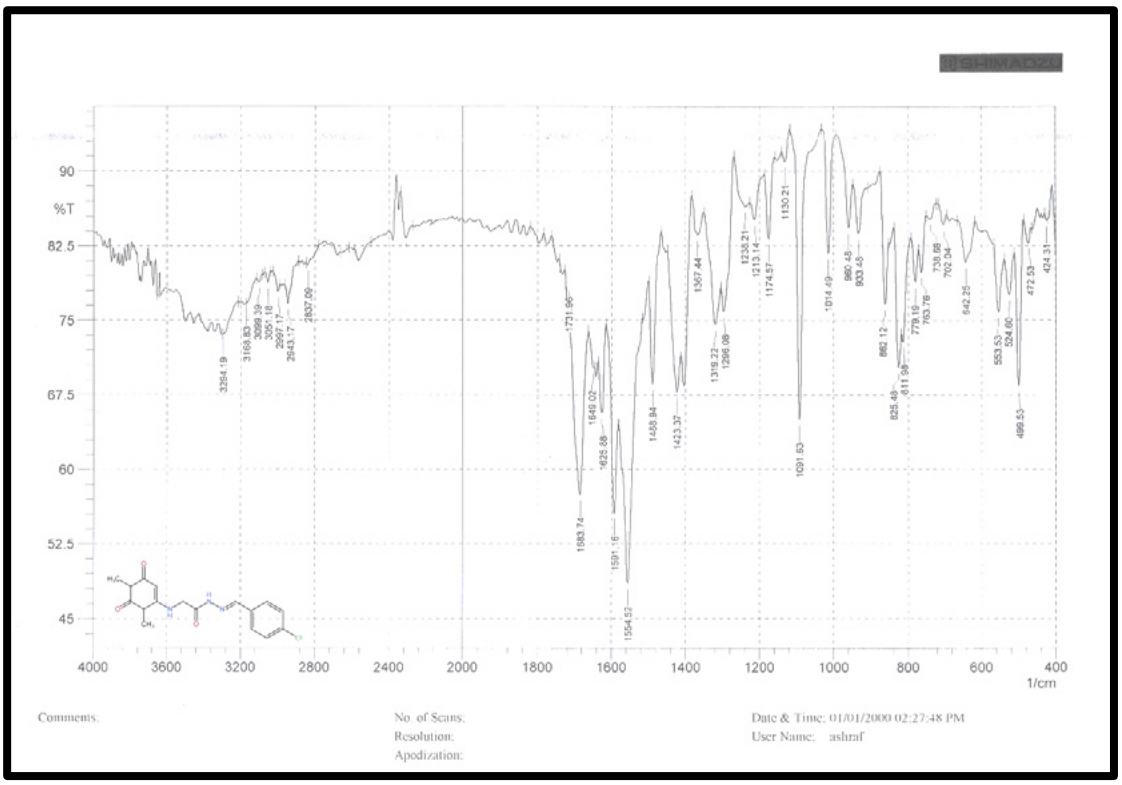

Figure 3. FTIR Soectrum of Compound (3)

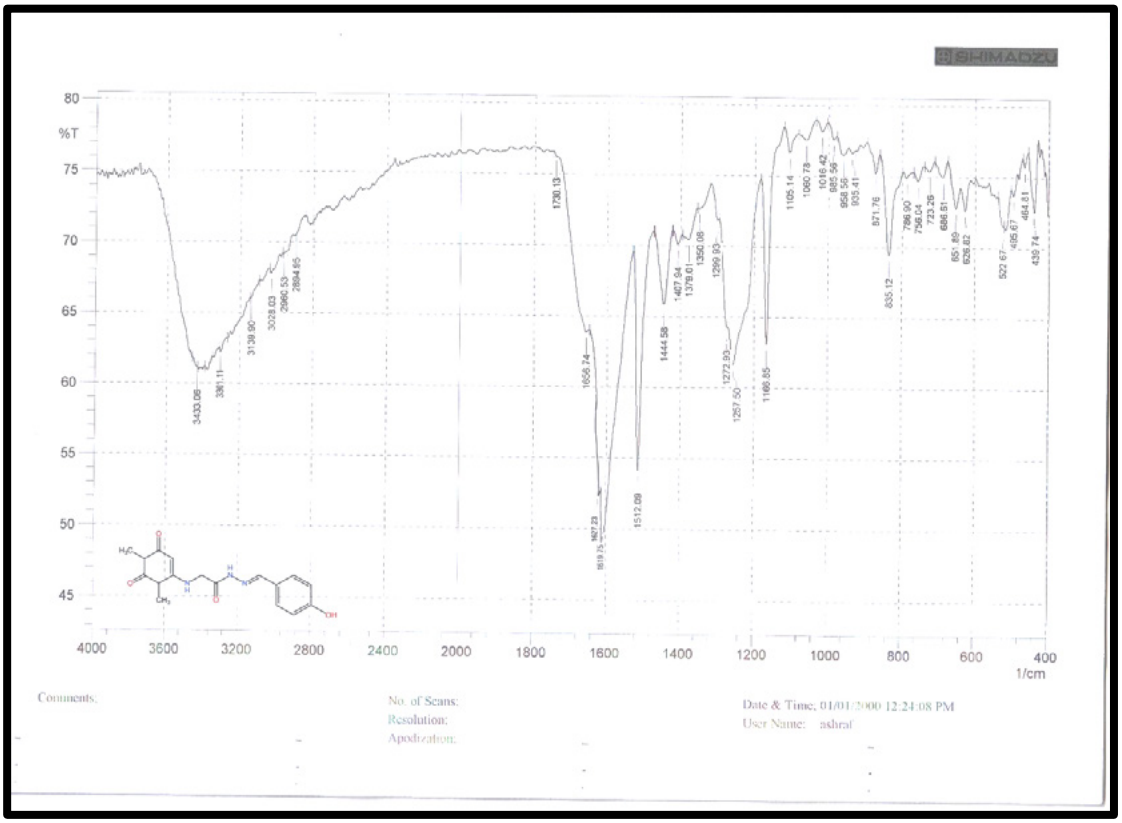

Figure 4. FTIR Soectrum of Compound (4)

https://doi.org/10.17993/3ctic.2023.121.83-116

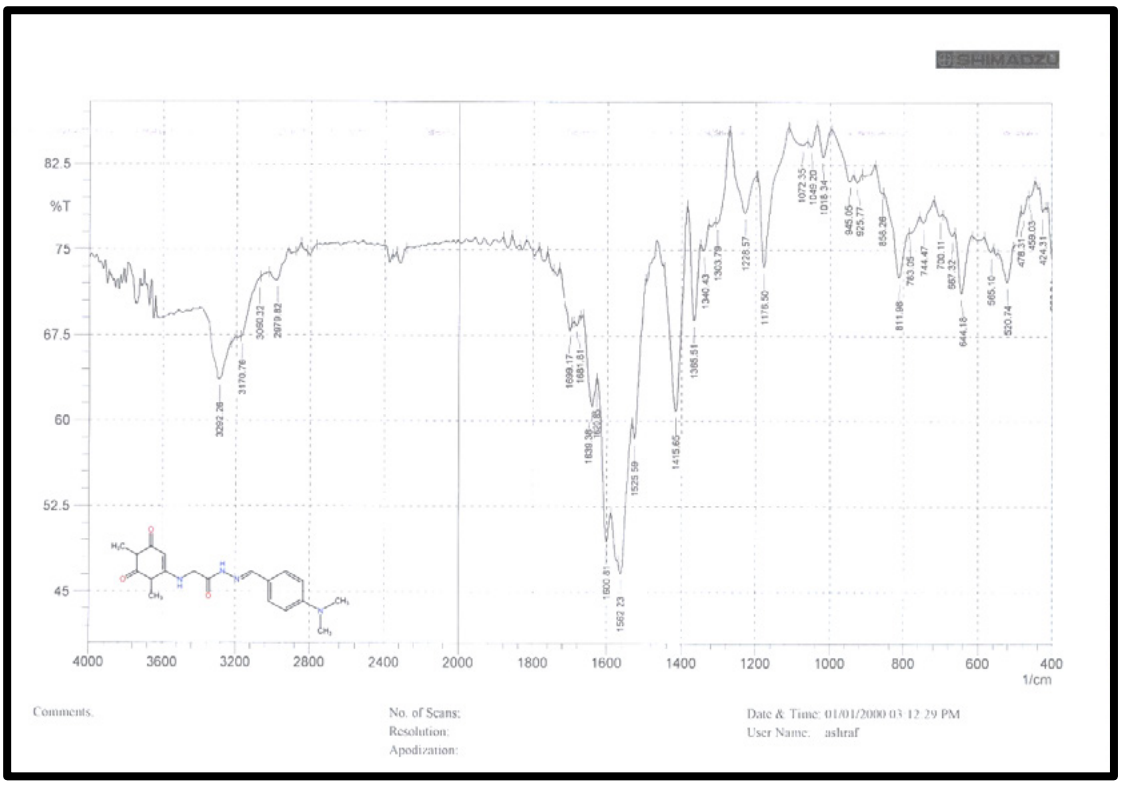

Figure 5. FTIR Soectrum of Compound (5)

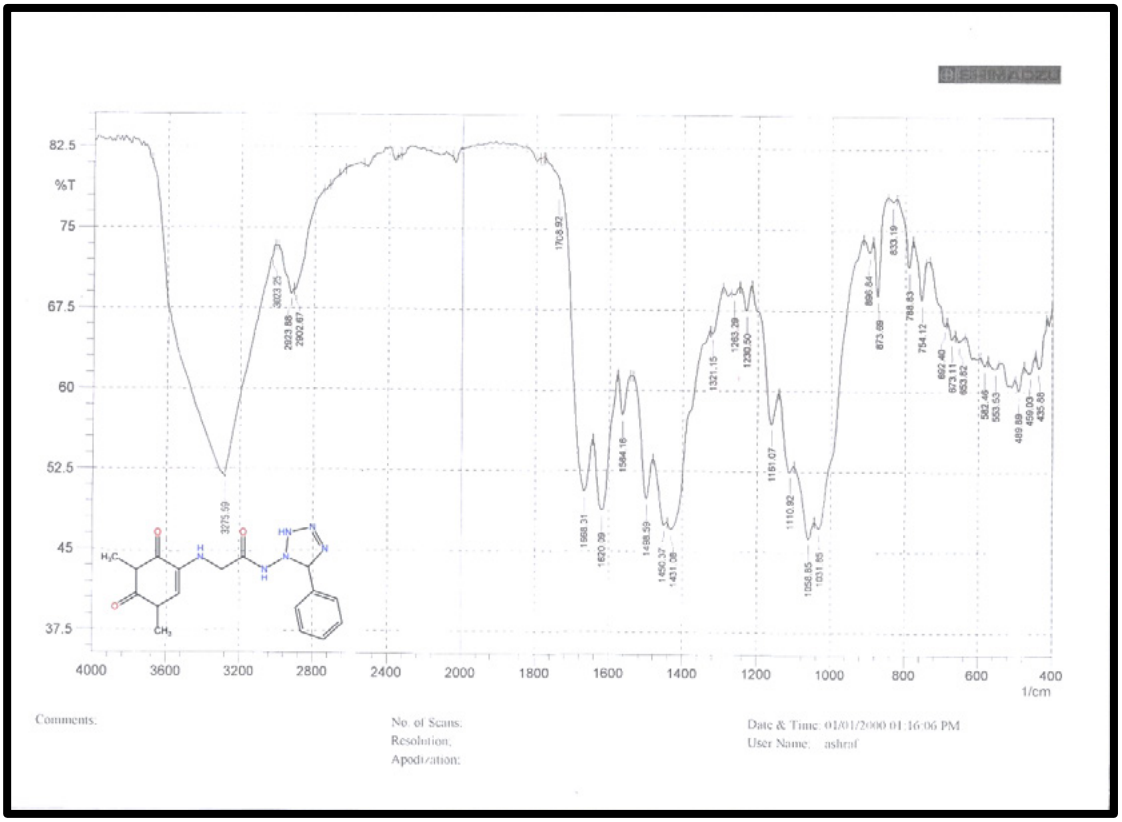

Figure 6. FTIR Soectrum of Compound (6)

https://doi.org/10.17993/3ctic.2023.121.83-116

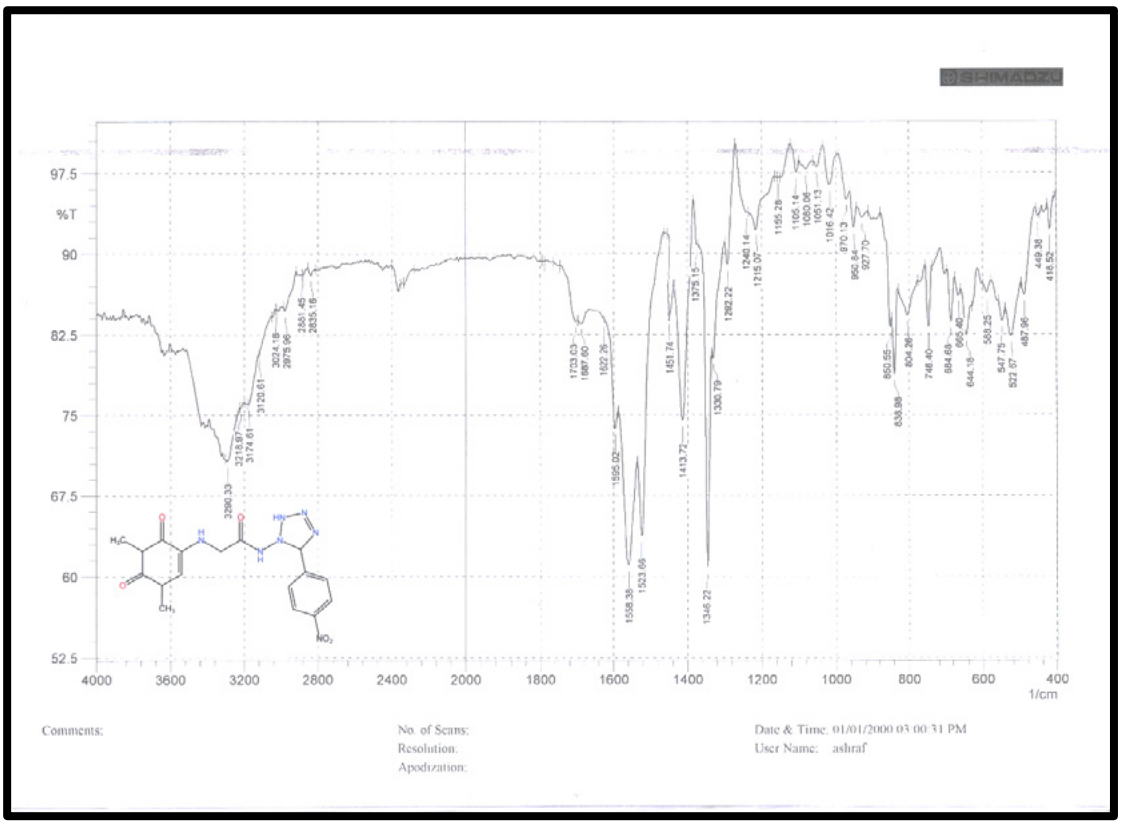

Figure 7. FTIR Soectrum of Compound (7)

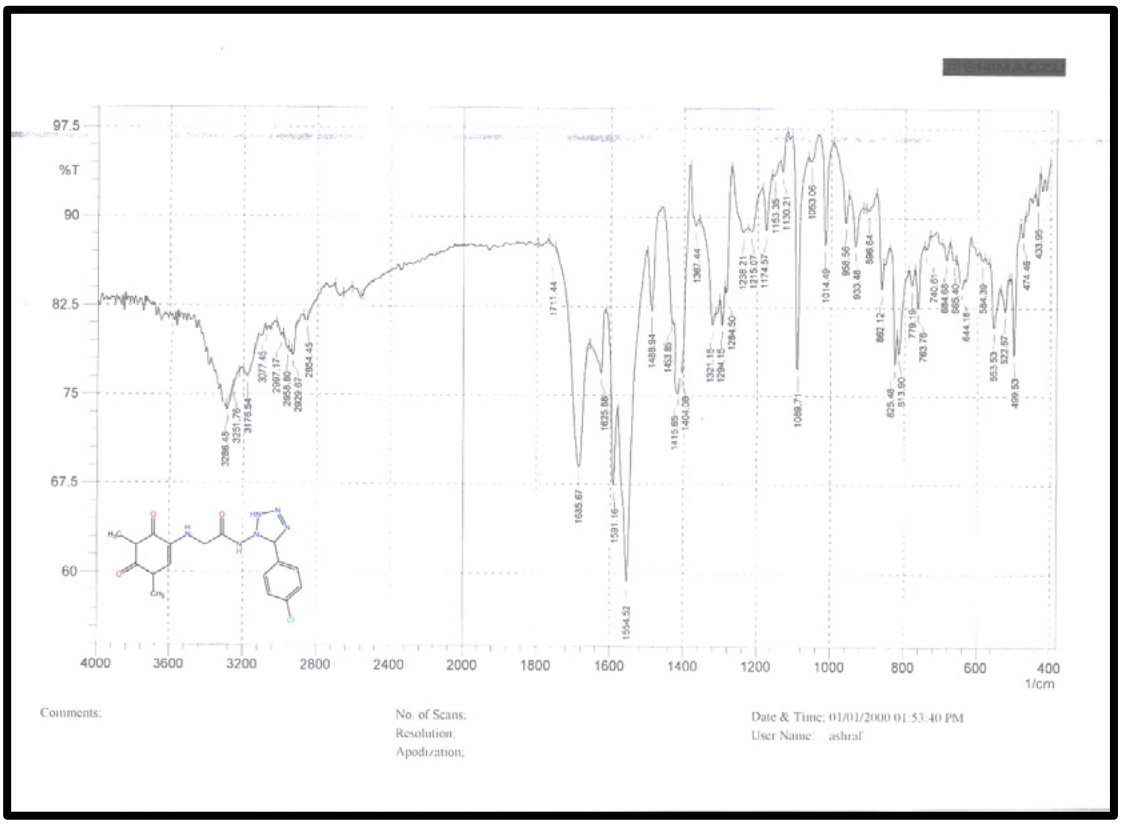

Figure 8. FTIR Soectrum of Compound (8)

https://doi.org/10.17993/3ctic.2023.121.83-116

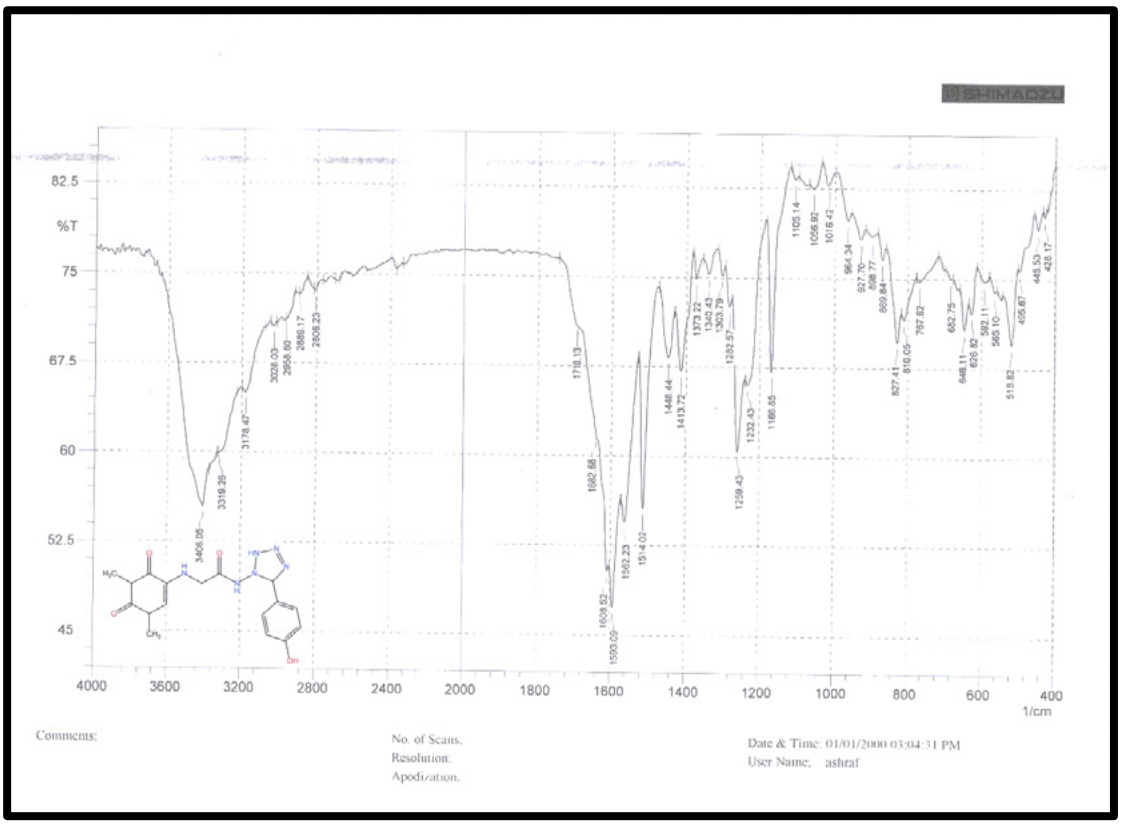

Figure 9. FTIR Soectrum of Compound (9)

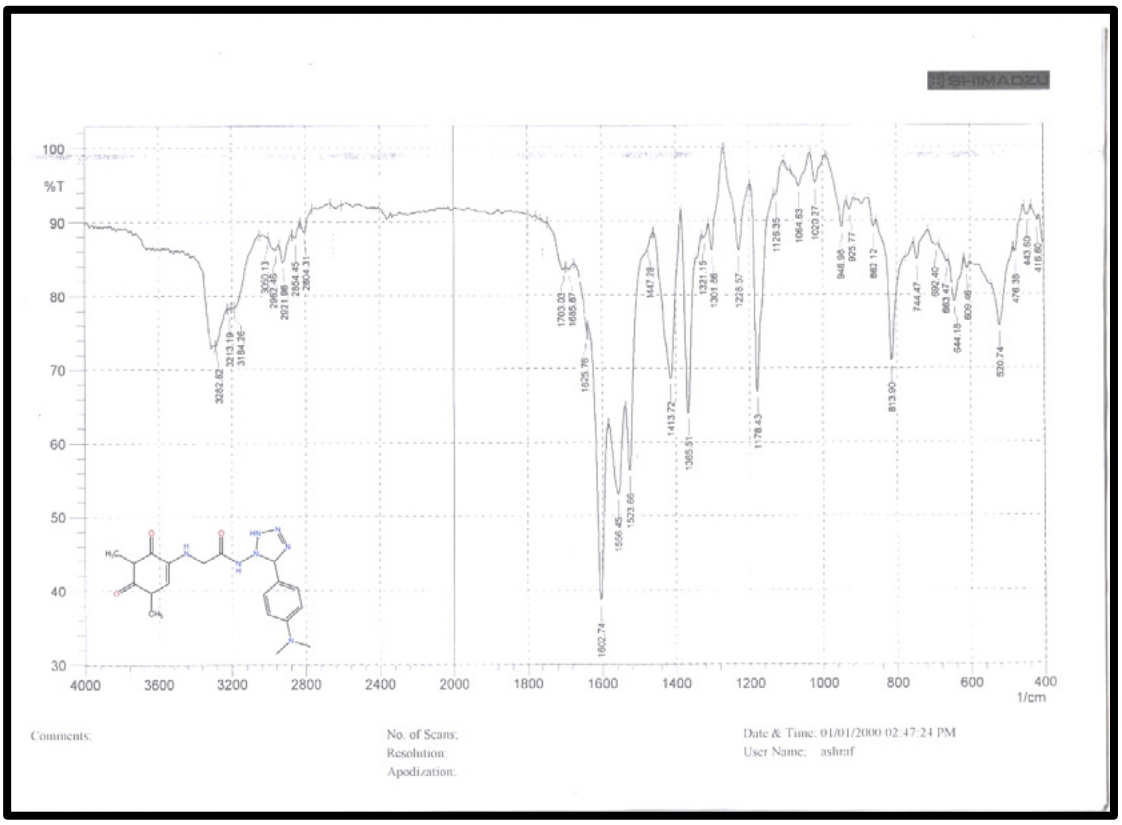

Figure 10. FTIR Soectrum of Compound (10)

https://doi.org/10.17993/3ctic.2023.121.83-116

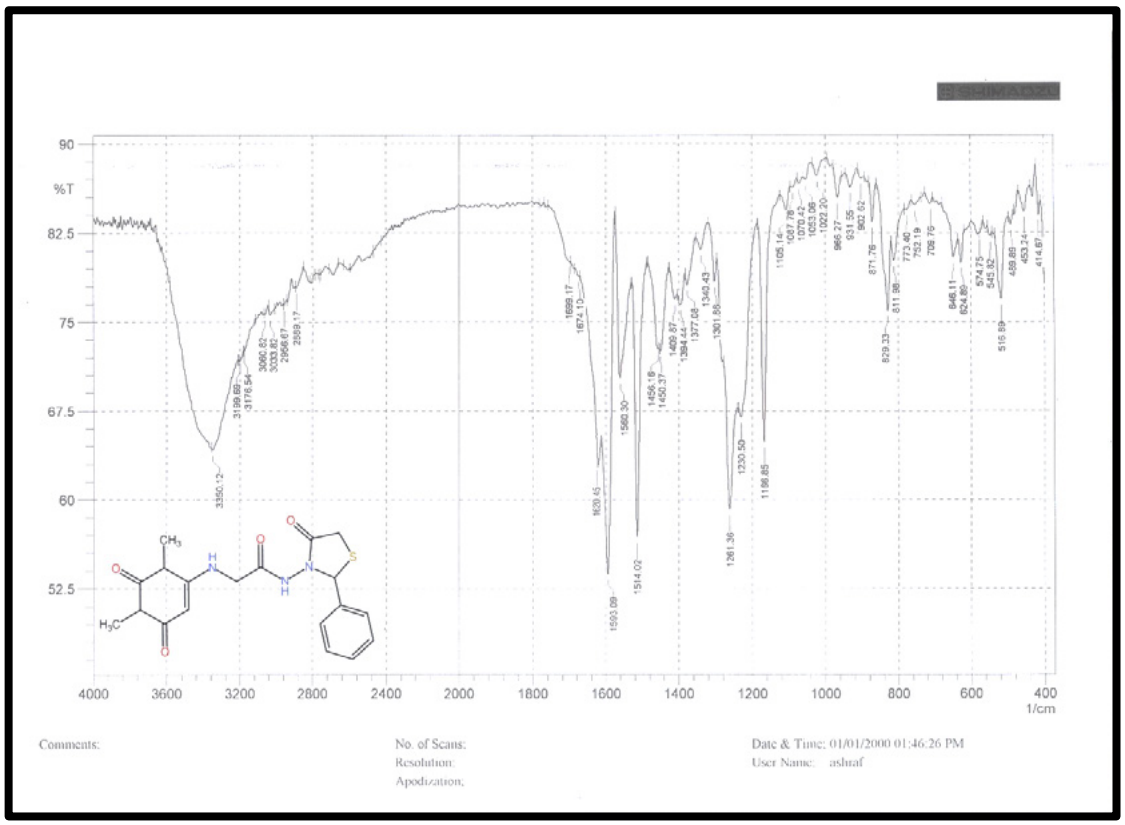

Figure 11. FTIR Soectrum of Compound (11)

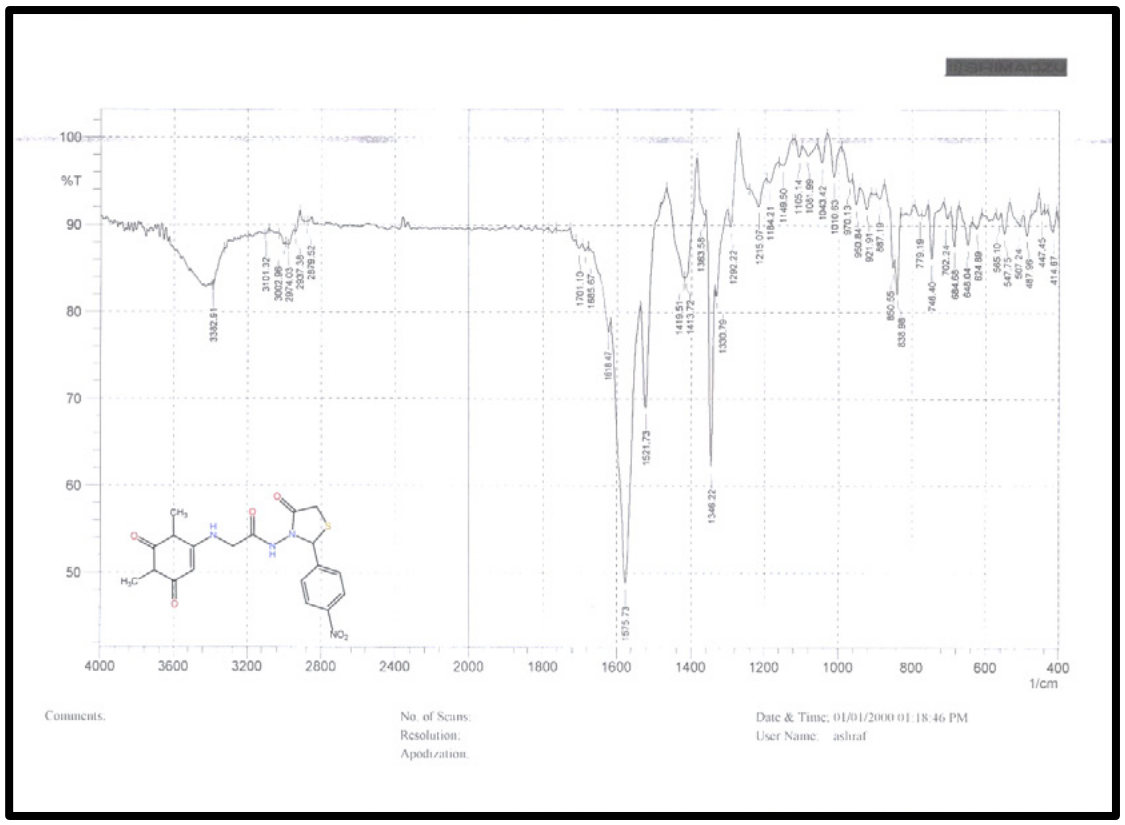

Figure 12. FTIR Soectrum of Compound (12)

https://doi.org/10.17993/3ctic.2023.121.83-116

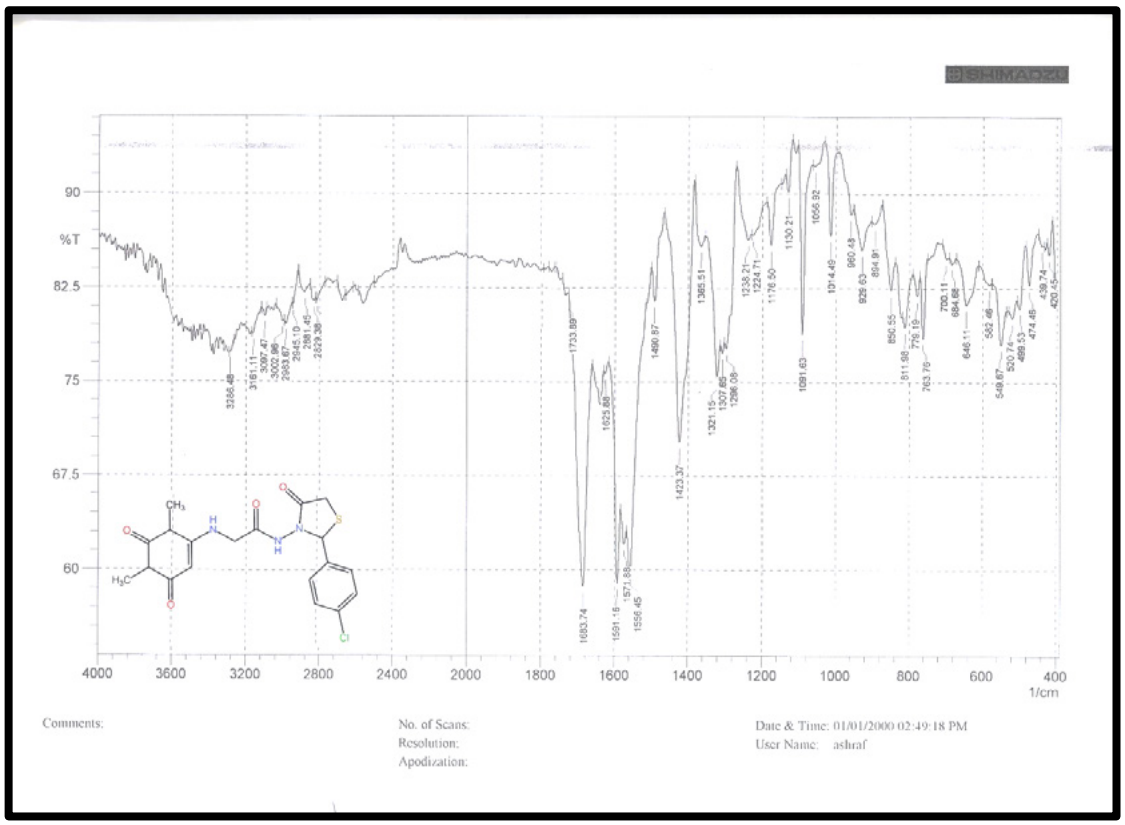

Figure 13. FTIR Soectrum of Compound (13)

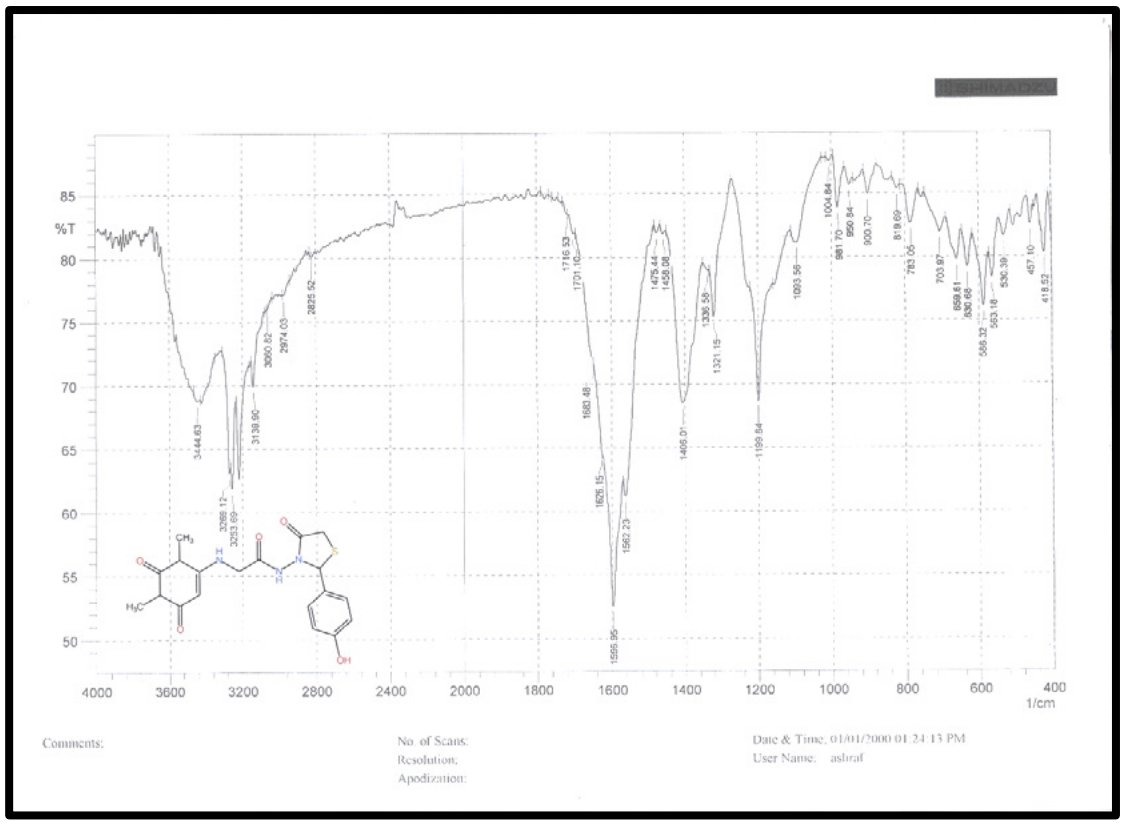

Figure 14. FTIR Soectrum of Compound (14)

https://doi.org/10.17993/3ctic.2023.121.83-116

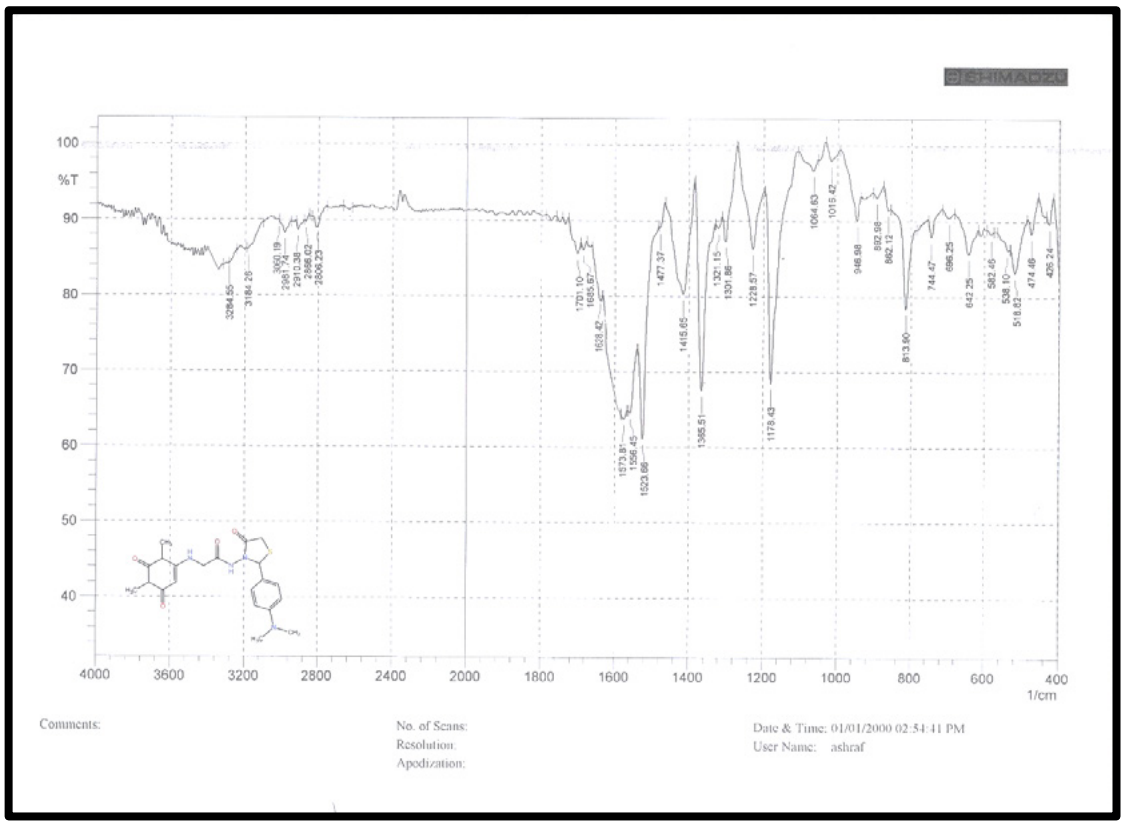

Figure 15. FTIR Soectrum of Compound (15)

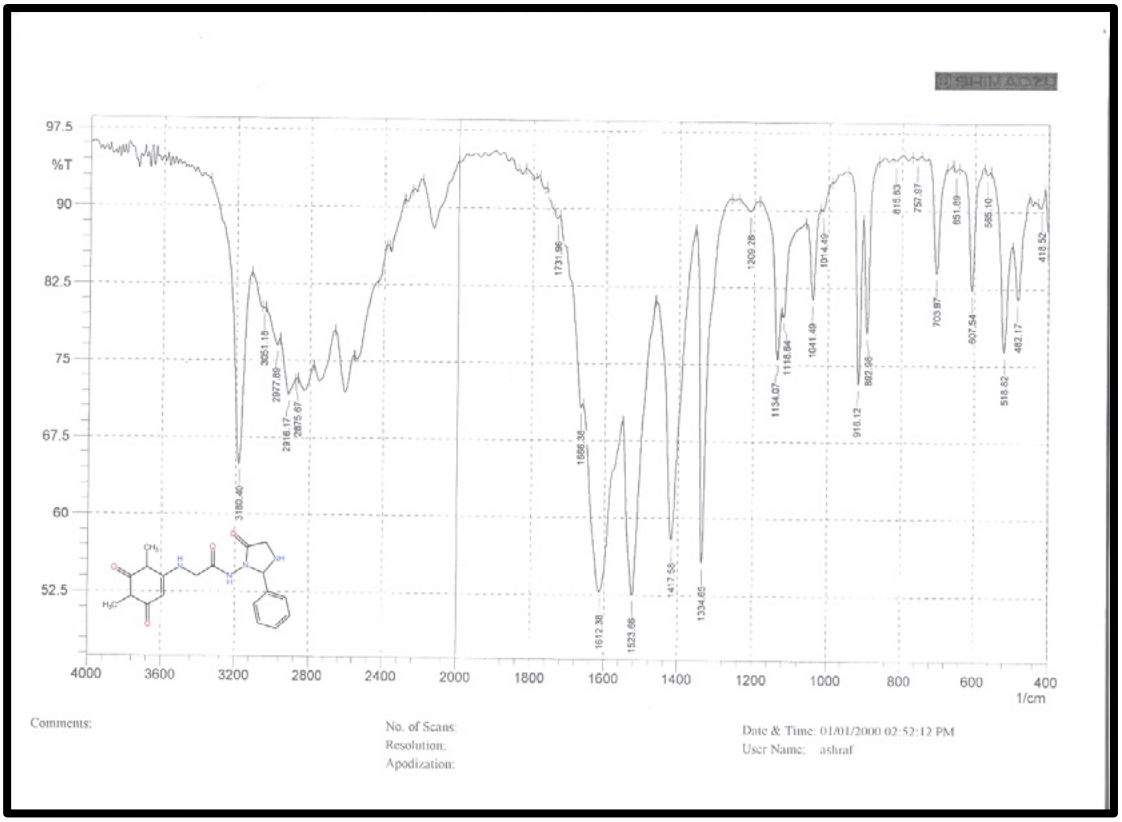

Figure 16. FTIR Soectrum of Compound (16)

https://doi.org/10.17993/3ctic.2023.121.83-116

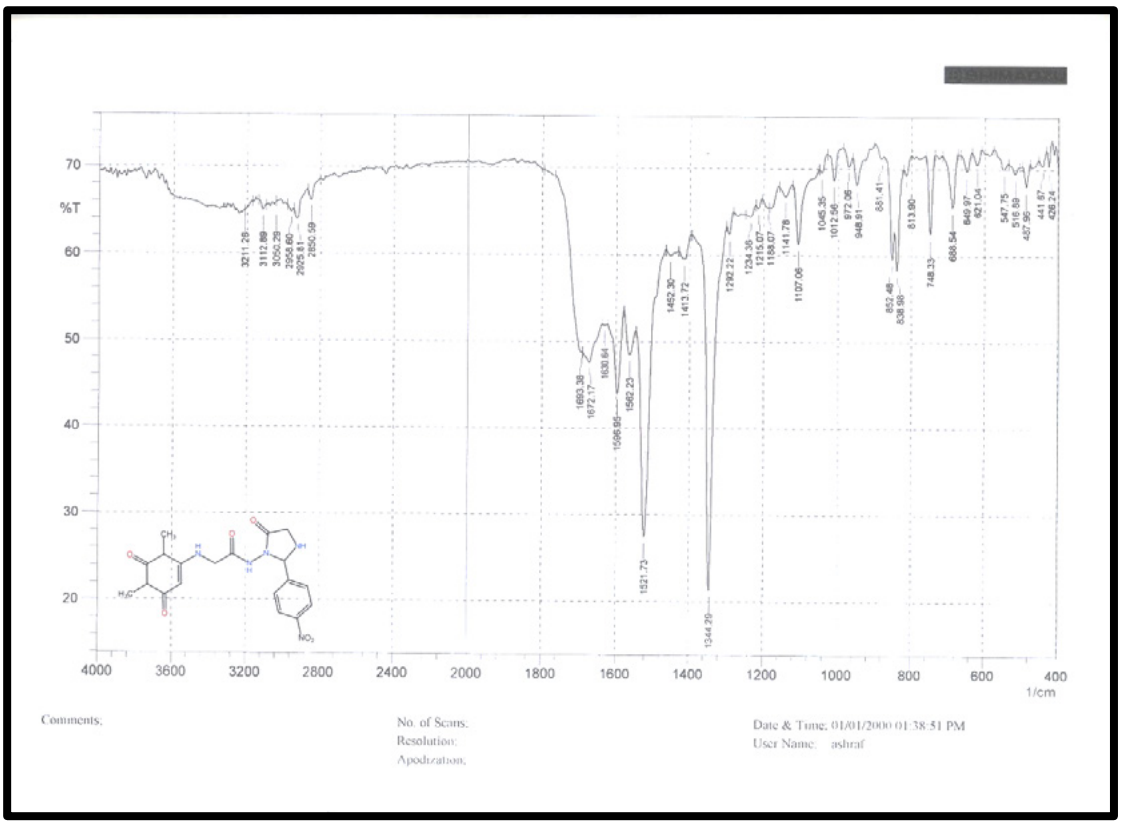

Figure 17. FTIR Soectrum of Compound (17)

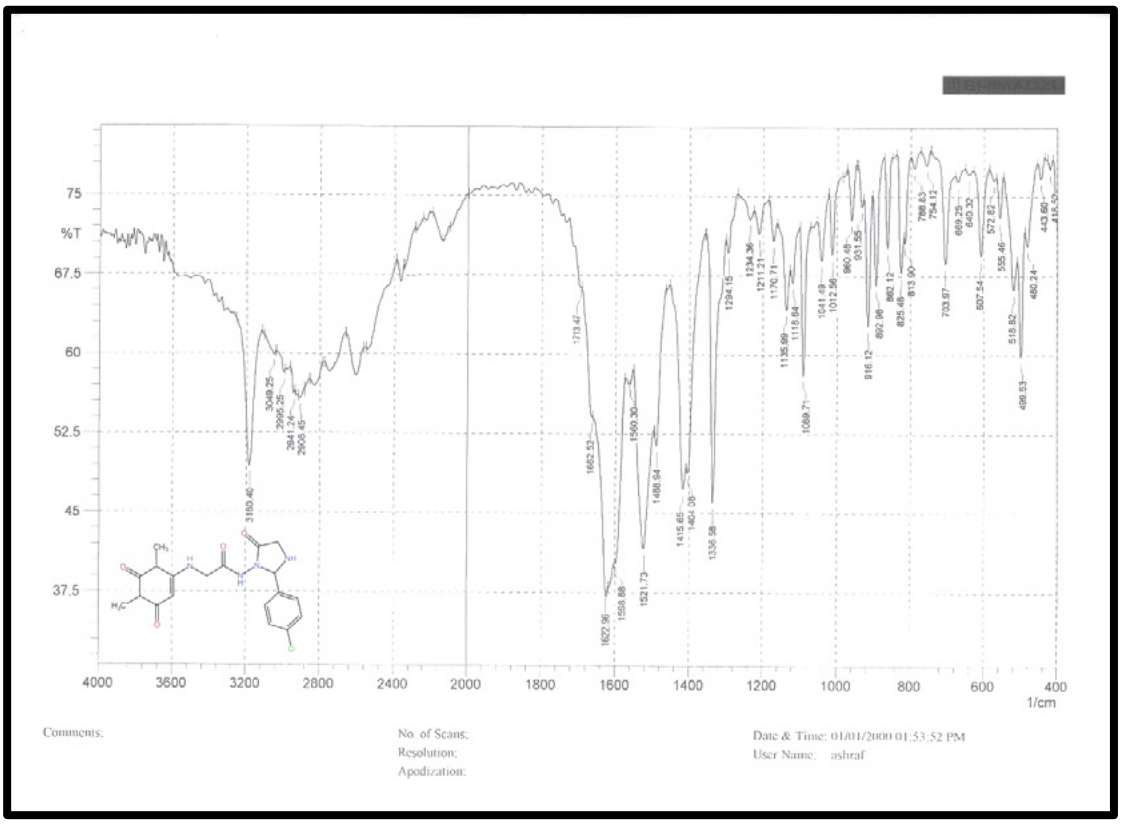

Figure 18. FTIR Soectrum of Compound (18)

https://doi.org/10.17993/3ctic.2023.121.83-116

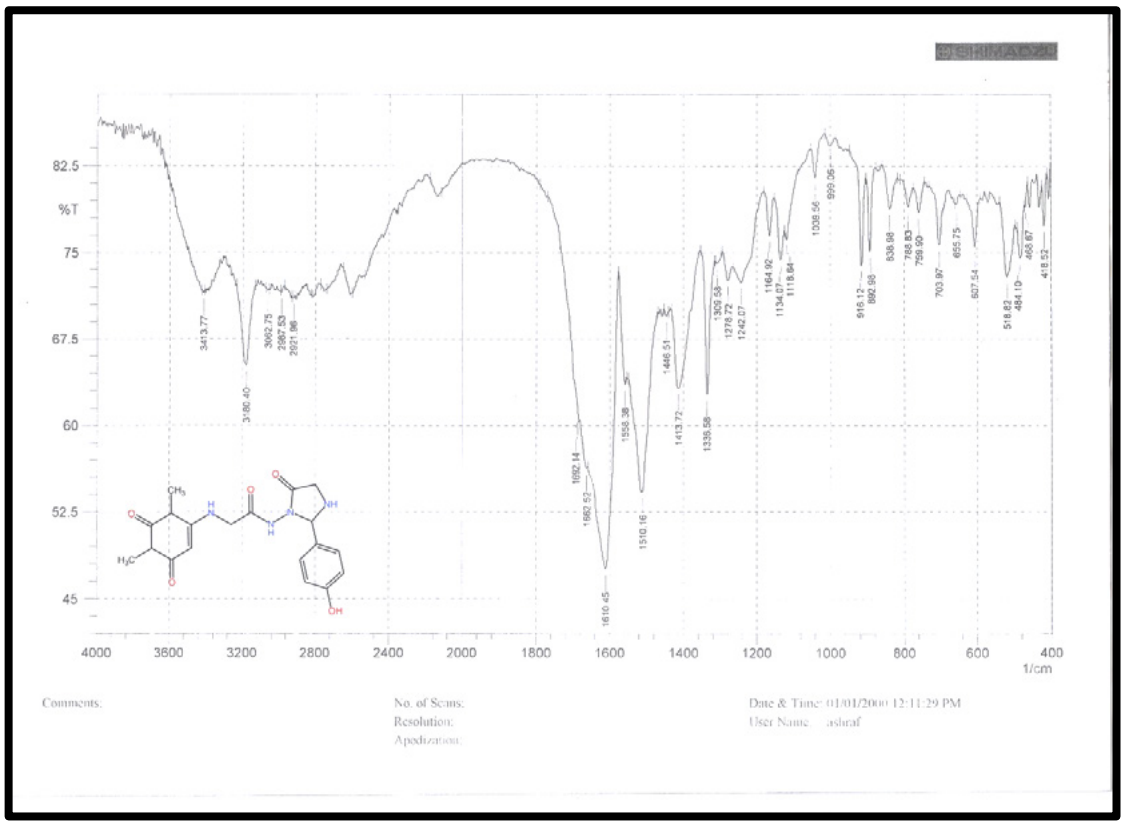

Figure 19. FTIR Soectrum of Compound (19)

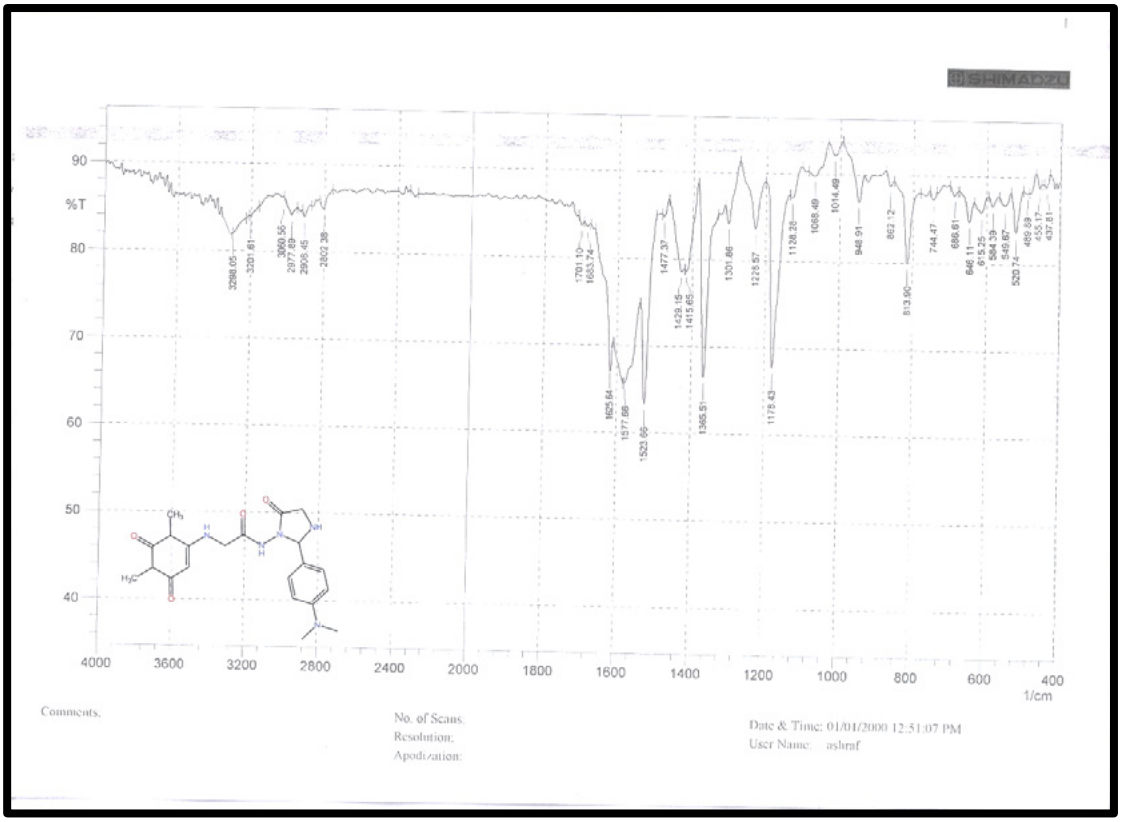

Figure 20. FTIR Soectrum of Compound (20)

https://doi.org/10.17993/3ctic.2023.121.83-116

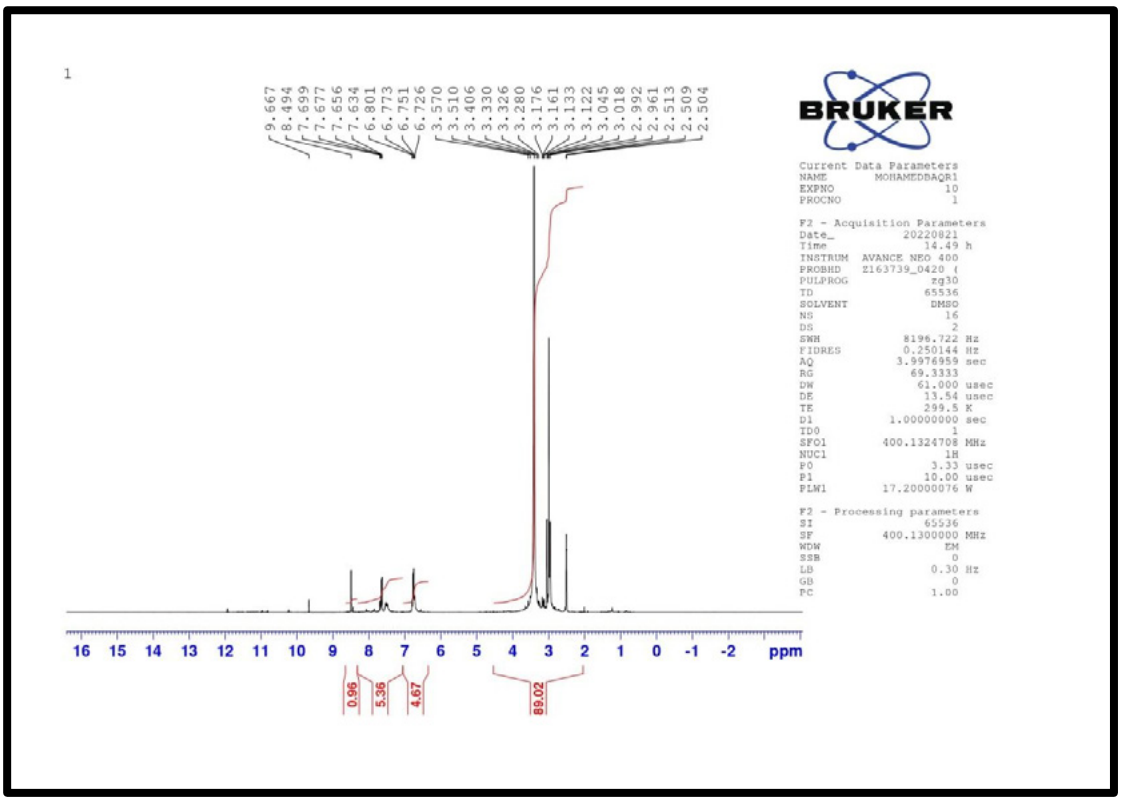

Figure 21. 1H-NMR of compound (5)

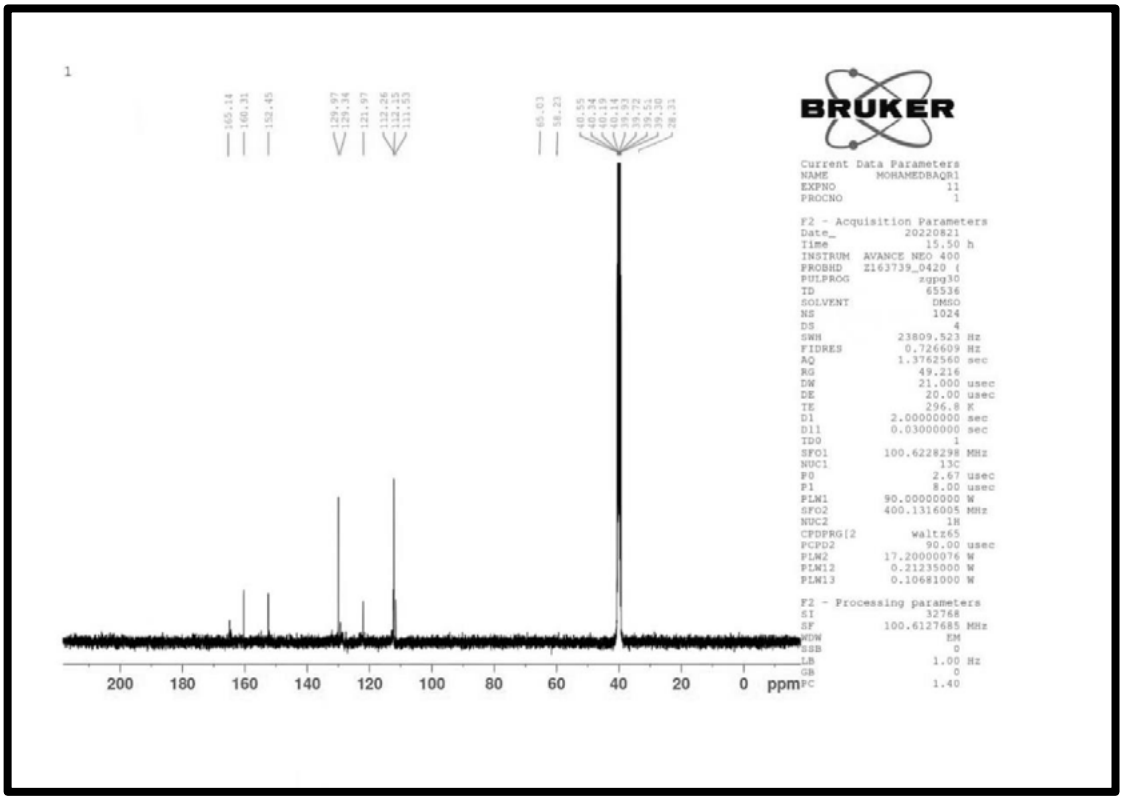

Figure 22. 13C-NMR of compound (5)

https://doi.org/10.17993/3ctic.2023.121.83-116

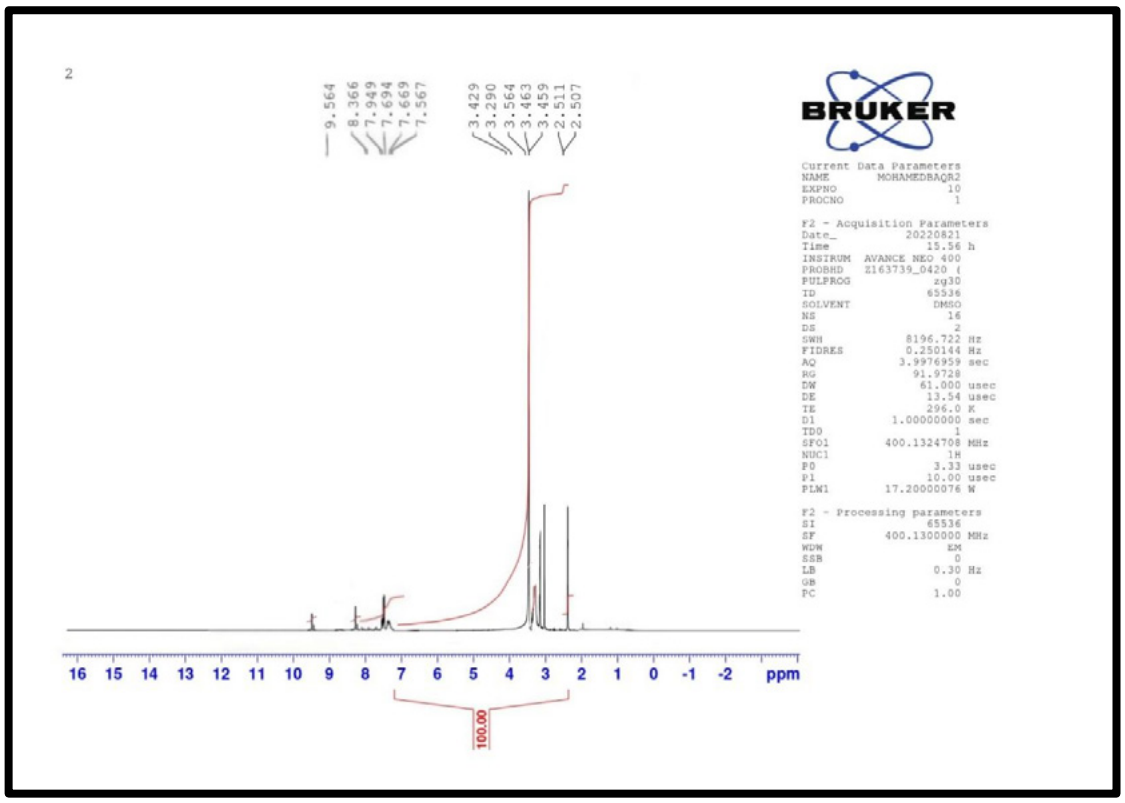

Figure 23. 1H-NMR of compound (7)

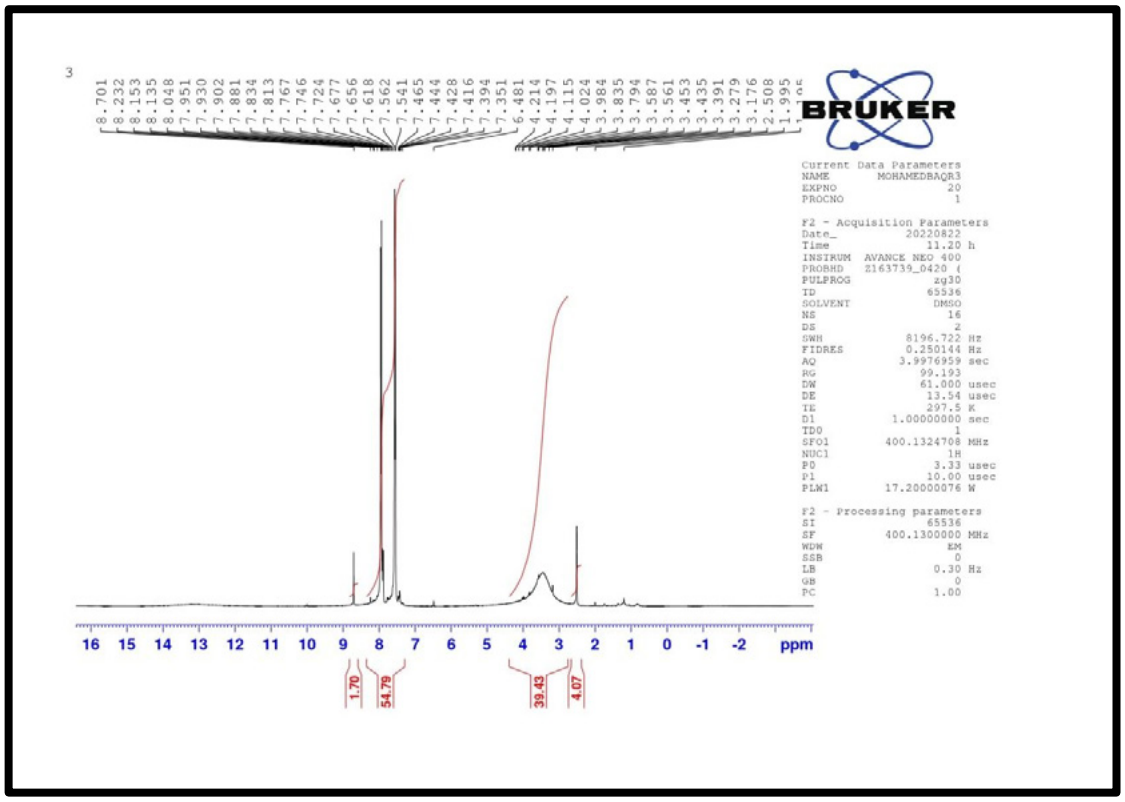

Figure 24. 1H-NMR of compound (13)

https://doi.org/10.17993/3ctic.2023.121.83-116

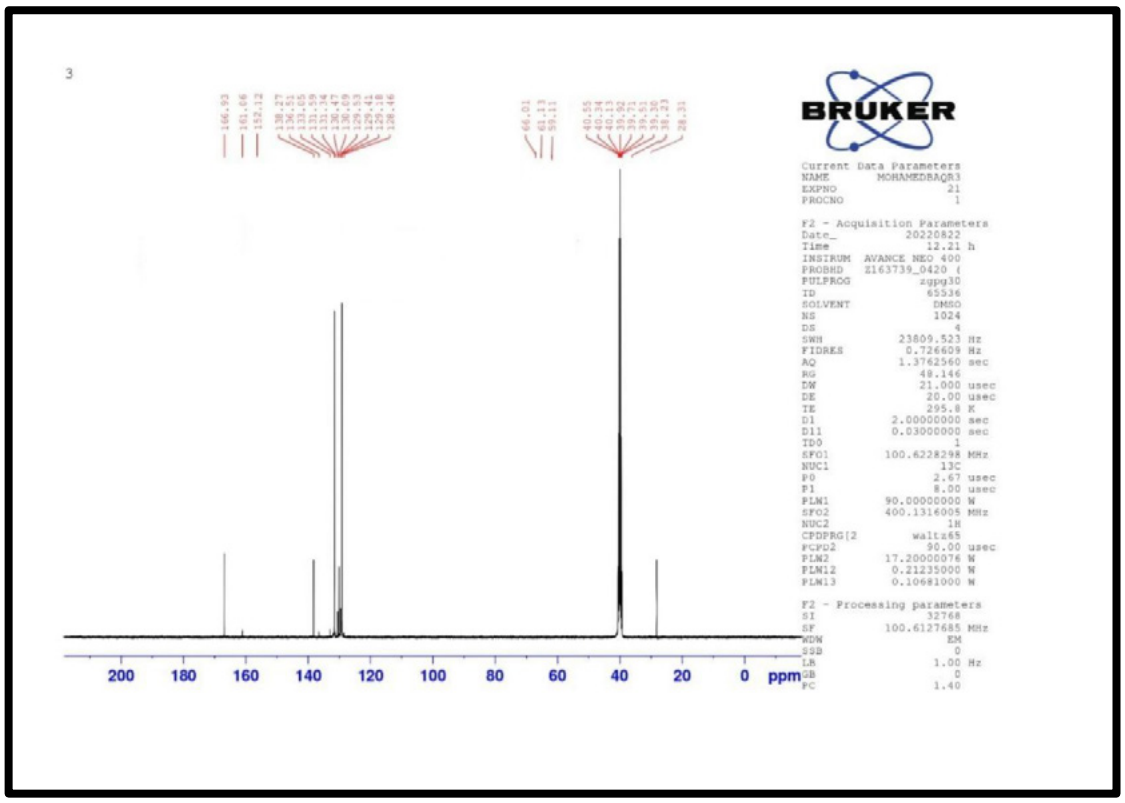

Figure 25. 13C-NMR of compound (13)

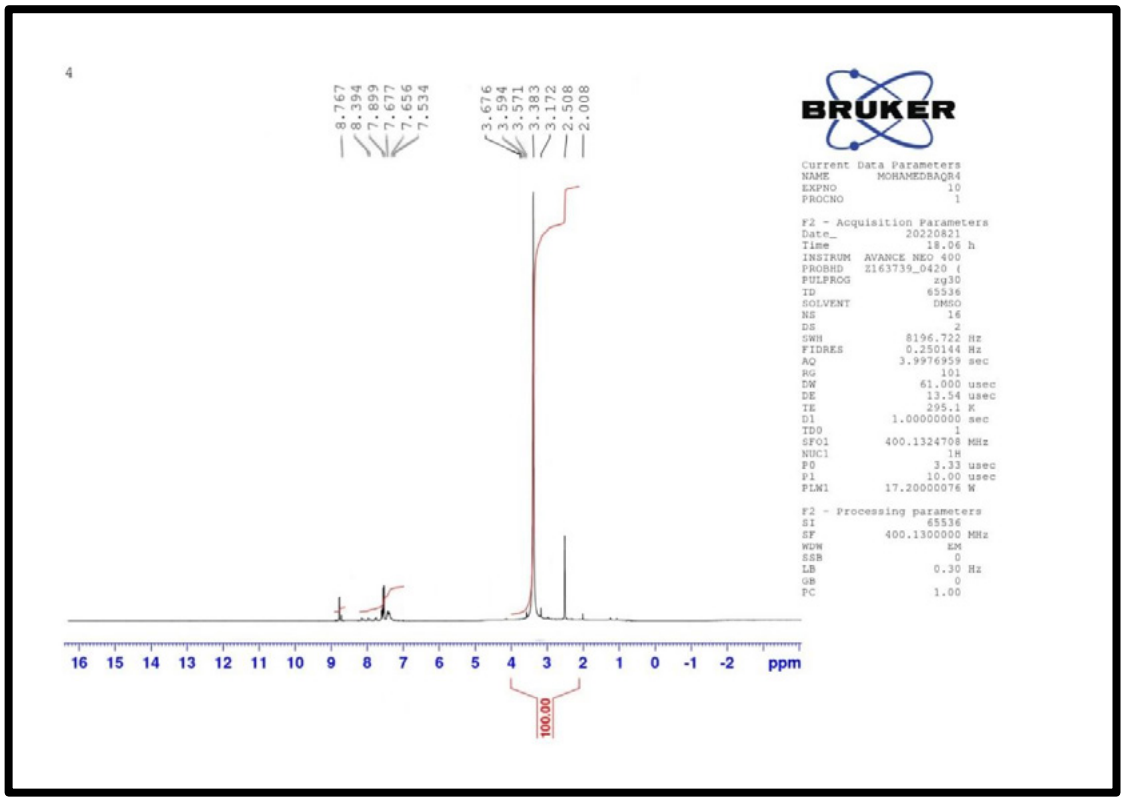

Figure 26. 1H-NMR of compound (16)

https://doi.org/10.17993/3ctic.2023.121.83-116

3.2. DPPH SCAVENGING ACTIVITY

All of the produced compounds (1-20) were either as active as the ordinary ascorbic acid or somewhat less active. The quantities of 50, 100, and 150 g /ml were used in a (2,2-diphenyl-1-picrylhydrazyl) test. The ultimate result is stoichiometric in terms of the number of electrons caught, It can be differentiated from others by either a changing in the dark violet hue of its exterior (DPPH) or a complete loss of color. We see a clear decline in efficacy with decreasing concentration in these prepared samples. Antioxidant activity was highest for component (11) at a concentration of (150 g/ml), as was out by reviewing the various results. An illustration of the newly synthesized compound's DPPH scavenging activity (1-20) is shown in Figure 27.

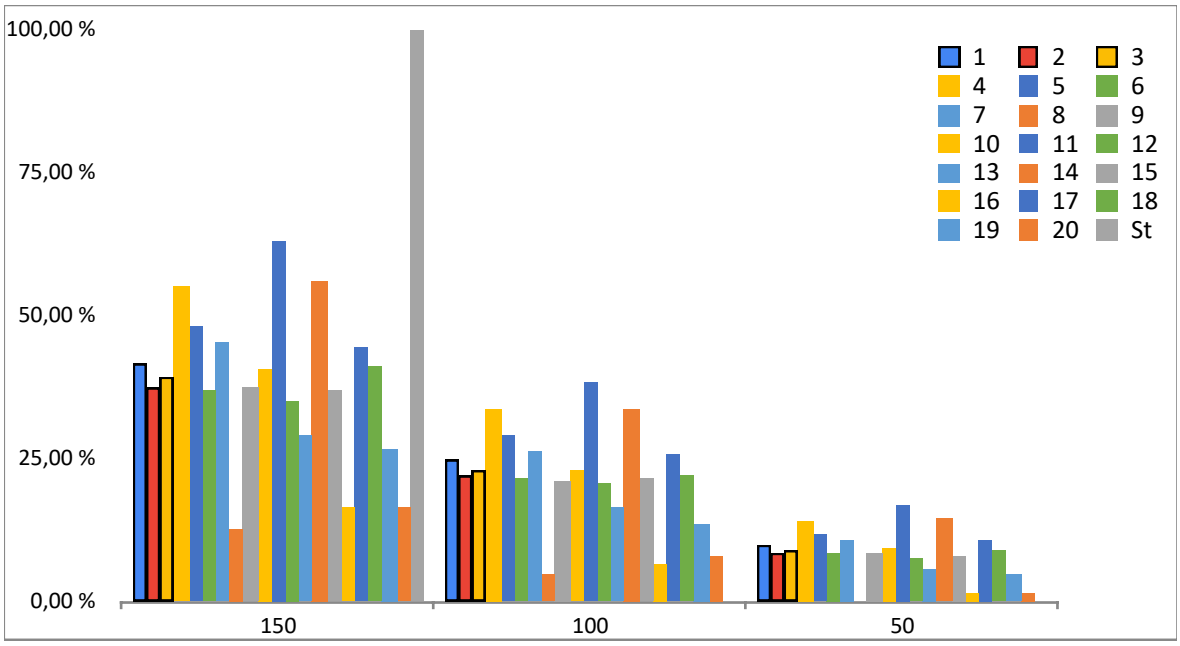

Figure 27. New compound's DPPH-scavenging action(1-20)

3.3. QUANTITATIVE MEASURE OF ANTIOXIDANT CAPACITY

The phosphomolybdenum method was used to calculate the combined antioxidant power of all synthesized compounds (1–20). This technique relies on the ability of synthesized compounds to convert colorless 70 Molybdenum(VI) to colored Molybdenum(V) via the formation of a green phosphate - Mo(V) complex at acidic pH. The chemical was found to have significantly higher antioxidant activity than ascorbic acid. Among the recently synthesized uracil derivatives, compounds (1-20) exhibit a low antioxidant ability against decreased Mo(VI) to Mo(V), as depicted in Figure 28.

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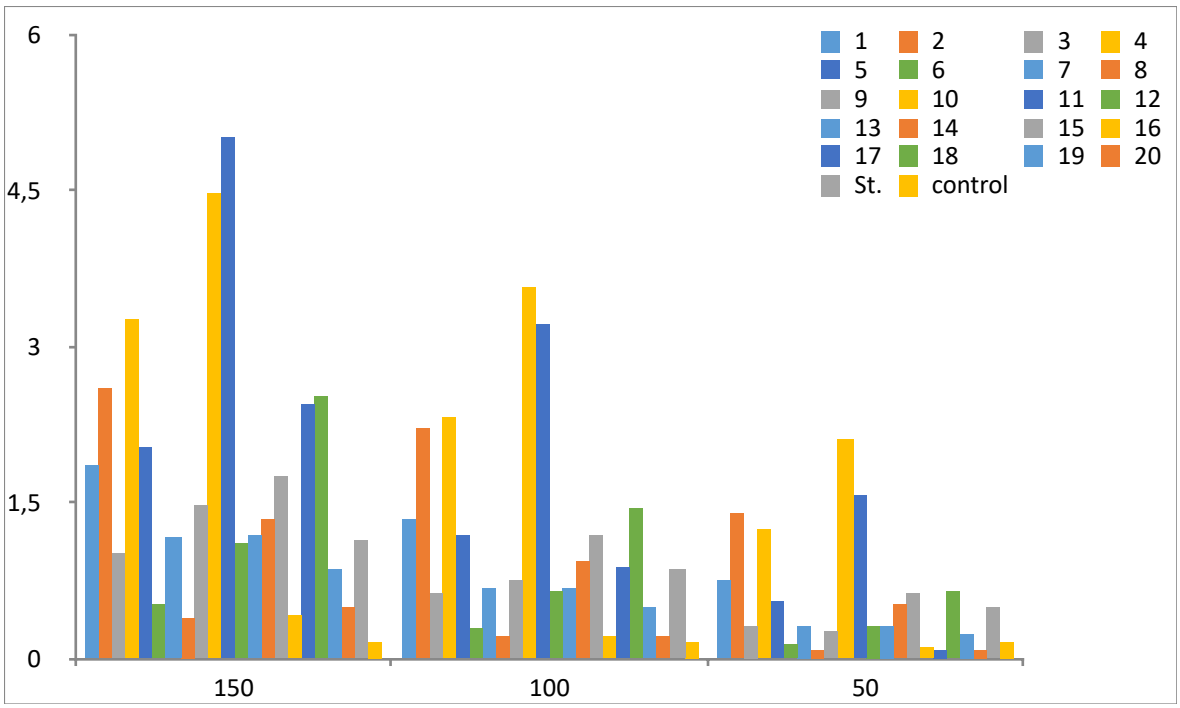

Figure 28. Total antioxidant capacity of the newly synthesized compound (1-20)

3.4. DOCKING STUDIES

To provide light on why synthetic substances have antioxidant properties (1-4, 6-11 and 13-20). Aromatase, an enzyme protein implicated in breast cancer etiology and induction, was one of many pharmaceutical targets subjected to docking studies. The crystal structure of Aromatase's crystal structure (PDB id: 3S7S) in association with the reference drug Exemestane was obtained from the Protein Data Bank (EXM).

There are docking studies shown in Table 5. Compared to the reference medication Exemestane, compounds (1–4, 6–11, and 13–20) showed a more stable fit into the aromatase binding pocket through interactions with critical residues ARG 115, PHE 221, TRP224, ASP309, MET374, HIE 480, and HEM600.

When compared to the reference compound (-3.657 kcal/mol) in table-7, compound (14) has a dock score of -7.139 kcal/mol. The docking score is higher here than it is for co-crystalline.

So, these relationships help to clarify the decline in aromatase activity. This work adds to the growing body of evidence that the synthesized chemicals have potential as a new class of chemotherapeutic medications for the treatment of breast cancer and other associated illnesses. Several compounds' structures are shown in Figure 29.

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Table 7. Consequences of molecular docking of compound (1-4, 6-11, and 13-20)

Compounds	Types of residues	Docking score	Glide Energy
1	PHE 221, HIE 480	0.740	-16.33
2	ARG 115, PHE 221, MET 374, HIE 480	0.767	-10.996
3	HEM 600	-1.735	-37.043
4	TRP 224, MET 374, HEM 600	-5.530	-24.171
6	PHE 221, TRP 224, MET 374, HEM 600	-6.486	-44.412
7	MET 374, HEM 600	-1.045	-48.6
8	ASP 309, MET 374, HEM 600	-3.503	-30.517
9	PHE 134, MET 374, HEM 600	-4.456	-31.474
10	MET 374, HEM 600	-2.910	-39.268
11	TRP 224	-5.786	-37.608
13	HEM 600	-3.900	-39.437
14	MET 374, HEM 600	-7.139	-29.686
15	HEM 600	-1.166	-24.856
16	TRP224, MET 374, HEM 600	-5.548	-43.625
17	ARG 115, HEM 600	-3.685	-35.37
18	MET 374, HEM 600	-5.050	-26.56
19	HEM 600	-4.892	-34.777
20	MET 374, HEM 600	-5.181	-47.623
Standard	MET 374	-3.657	-18.206

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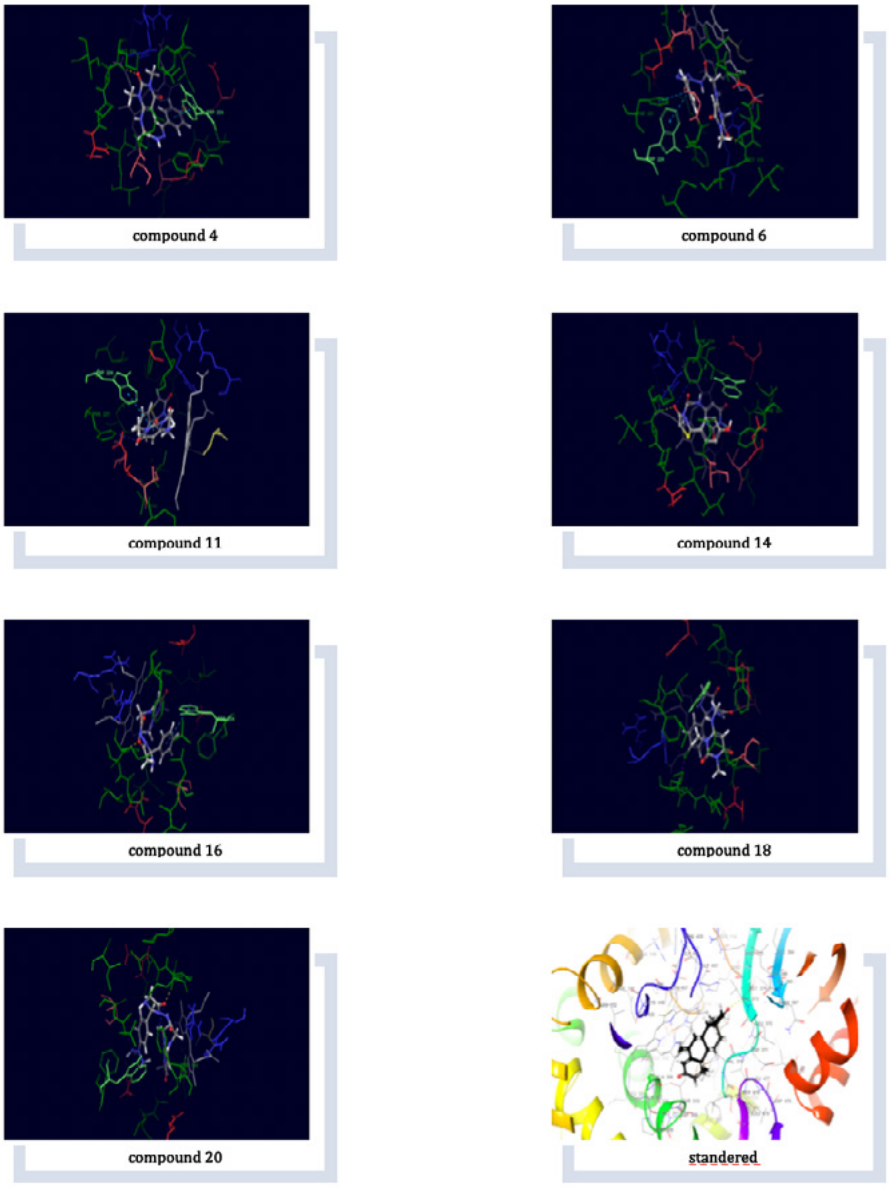

Figure 29. View docking Molecular of some compounds and standard

4. CONCLUSION

In this work, synthesis new heterocyclic compounds from reaction uracil derivatives with sodium azide, 2-mercapto acid & 2-amino acetic acid to produce five-membered heterocyclic rings includes: tetrazoline-1yl, thiazolidin-4-one and imidazolidin-4-one derivatives respectively. This compounds was measured biological activity by two types of anti-oxidant activity DPPH and phosphomolybdenum at three concentration (50, 100 150) ppm Results shown the phosphomolybdenum is batter worked of this compounds and the highest Values at 5.023 of compound (11) compare with standard 1.142 in concentration 150 ppm and study molecular docking shown Results The effectiveness of these compounds for the treatment of breast cancer and other associated diseases.

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