Evaluation Of Biological Activity For compounds Containing Thiazole Ring

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Abstract:
This study involves synthesis of new heterocycle compounds by many steps , the first is to react between 2-Amino-5-nitrothiazole with salicylaldehyde at 0^{o}Cand acid media to form azo derivative (1) , then react (1) with 4-hydroxyacetophenone to get chalcone derivative (2) , Third step involve react (2) with (hydrazine hydrate , phenyl hydrazine , 2,4-dinitrophenylhydrazine , hydroxyl amine hydrochloride ,urea , thiourea , ethyl cyanoacetate , malononitrile , guanidine) to form (Pyrazole derivatives (3,4,5) all these compound diagnosed by FT-IR spectrum ,^{1}H-NMR , ^{13}C-NMR ,CHN , and subsequent reaction by R_f - TLC and measurement liquefaction point .Then study the biological action for eleven compounds towards two kinds of microorganisms .

Keywords: thiazole, Pyrazole.

Introduction

Heterocyclic compounds represent a highly significant class of organic molecules, widely utilized across various domains such as dye manufacturing, pharmaceuticals, agriculture, and medicine. Due to their versatile structures and biological relevance, I have synthesized multiple derivatives belonging to this category for further investigation and application [1,2]. Pyrazoles are five-membered heterocyclic compounds containing two nitrogen atoms and three adjacent carbon atoms. Their derivatives exhibit a range of pro mising pharmacological and biological activities, including fungicidal, antitumor, anti microbial, herbicidal, virucidal, and insecticidal properties. [3–5].

EXPERIMENTAL

Materials and Instrumental analysis

All compounds are equipped from BDH , Aldrich and sigma chemical companies. (FTIR) Spectra (4000-400cm^{-1}) in KBr disk are registered on a Shimadzu FTIR-8400S Fourier .transform. the liquefaction point was defined using Stuart, UK. ^{1}H-NMR and ^{13}C-NMR spectra are gained with a model Bruker AM(400MHz)spectrometer for utilizing DMSO-d6 solvent in a suitable deuterated solution . Primary analysis (C.H.N.S) were achieved employing a C.H.N EA-99 mth tool. The purity of all compounds evaluated by thin film chromatography (TLC) utilizing Whatman 250m silica gel plates as the stationary stage and methanol as developing solvent.

Preparation of 2-hydroxy-5-((5-nitrothiazol-2-yl)diazenyl)benzaldehyde .compound (1)[6]

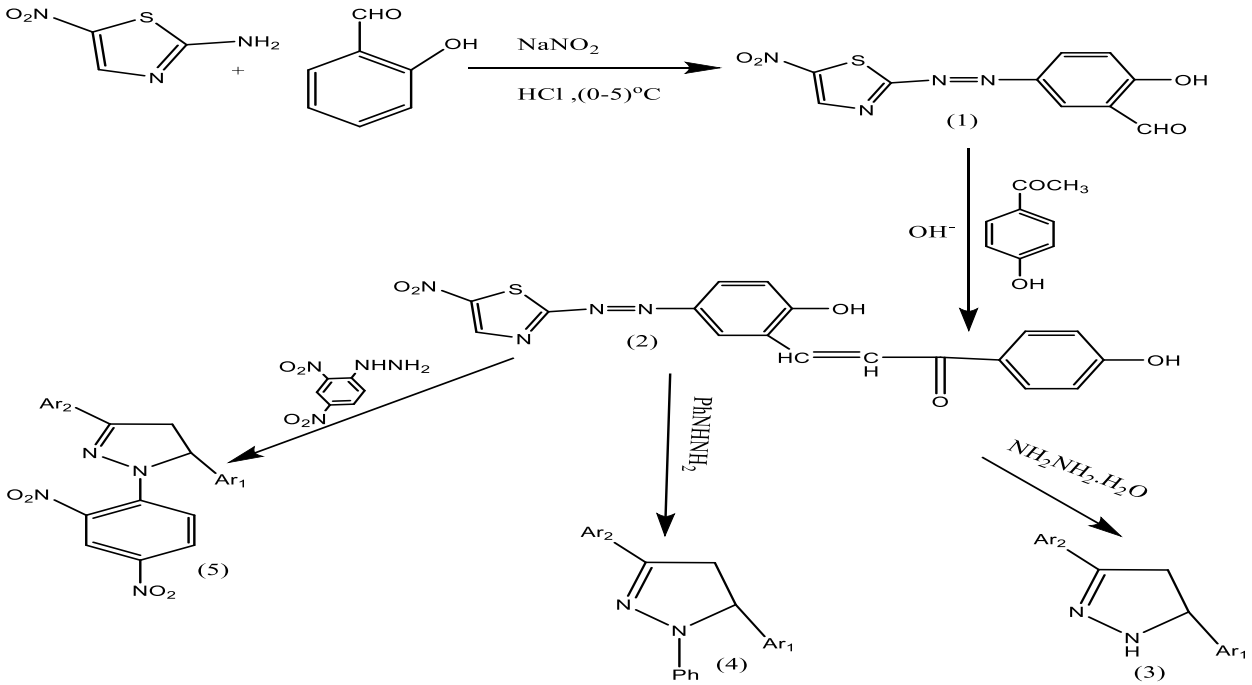
synthesized compound (1) by mixed of 2-amino-5-nitro thiazole (1.45gm,0.01mol) in 40 ml distilled water with 4 ml HCl . The solution is diazotized with (0.75 gm, 0.01 mol)in 20 ml distilled water sodium nitrate ($NaNO_2$) was cooled and supplemented slowly to a solution of 2-amino-5-nitro thiazole .The resulted reaction blend is moved of 25 minutes , made a brown solution .The resulted diazonium chloride solution was supplemented slowly with cooling condition and continuous moving at (0-5)^oC. The solvent of salicylaldehyde (0.01 mol) melted in (50) ml ethanol .The color of the reaction mass was altered from brown to red color. The reaction blend was moved for additional (2) hours at (0-5)^oC in ice-bath. After completing reaction, the reaction blend was supplemented to the ice cold water (200ml) with stirring .The crude produce is isolated by filtration , flushed with distilled water then desiccated .The solids gained recrystallized with ethanol to obtain red crystals.

***Preparation of 3-(2-hydroxy-5-((5-nitrothiazol-2-yl)diazenyl)phenyl)-1-(4-hydroxyphenyl) prop -2-en-1-one . compound* (2)**[7]

chalcone is made according to the hot concentration (0.1 mole) derivatives p-hydroxy acetophenone and (0.1 mole) compound(1) are solved in least quantity of ethanol, 55 ml of 50% potassium hydroxide is supplemented to the aforementioned solvent. The flask is heated at 50 ^oC for 20 hours. The solvent is acidified by cold 6 N HCl solvent (congored), crystal-like objects isolated, that is purified and flushed with water. It is recrystallized from ethanol.

Preparation of (3-5) compounds [8]

In a 100 ml round bottom flask a blend of(0.01 mole) of Chalcone derivative(2) and (0.01mole) (hydrazine hydrate , phenylhydrazine and 2,4-dinitrophenyl hydrazine) in 50 ml of Ethanol absolute. with continuous stirring at 72C$^\circ$ for (7-12) h, the solvent was then removed and the resulting solid was recrystallized from ethanol to get (3,4 and 5) respectively .



Scheme 1 : Synthesis of compounds (1-11)

RESULT AND DISCUSSION

***2-hydroxy-5-((5-nitrothiazol-2-yl)diazenyl)benzaldehyde compound* (1)**

The infrared spectrum information of derivative (1) reveal absorption at (1735) cm^{-1} for (C=O), (1458) cm^{-1}(-N=N-),(3409) cm^{-1} (OH) for phenol, and display band at (3139) for (N-H)for imidazol, and Vanishing band for NH_2 at (3379-3325)cm^{-1} .The^{1}H-NMR(DMSO) spectrum data of derivative (1) display δ:6.7-8.9(m , 4H , Ar-H) , 9.11 (m , 1H , OH) ,13.8 (m , 1H,CH)Ald. . The^{13}C-NMR(DMSO) spectrum data reveal δ:196 (C10) , 167(C1) ,163(C2) ,159(C4) ,154(C7), 101-151(C-ar) .

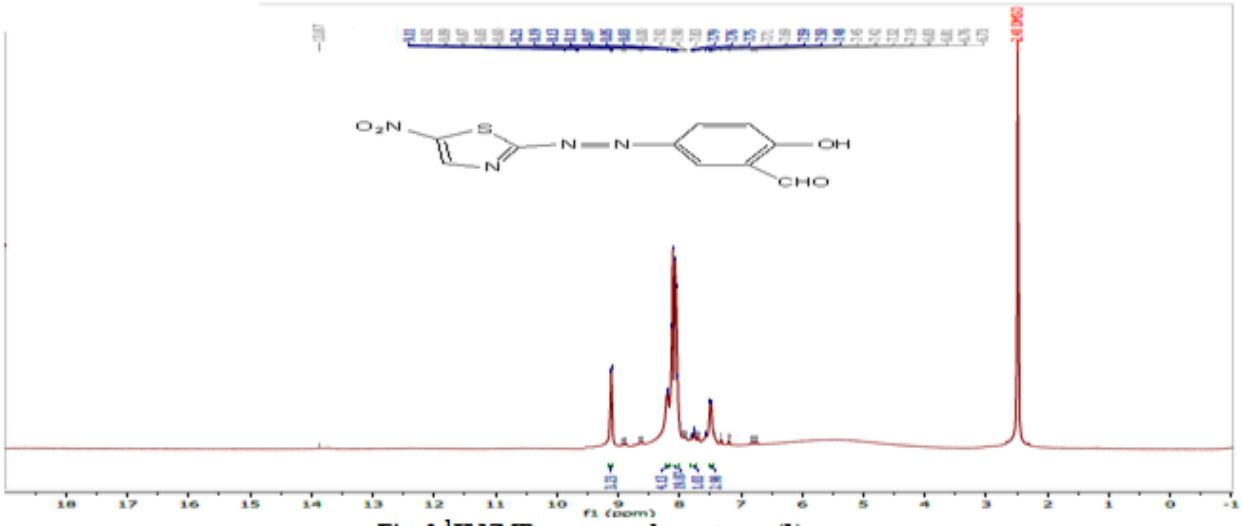


Fig .2 ^{1}H NMR compound spectrum (1)

***3-(2-hydroxy-5-((5-nitrothiazol-2-yl)diazenyl)phenyl)-1-(4-hydroxyphenyl)prop-2-en-1-one compound* (2)**

The infrared spectrum data of derivative (2) reveal absorption at (1730) cm^{-1} for (C=O),(1442) cm^{-1} (-N=N-),(3393) cm^{-1} two groups of (OH) for phenol, and .The^{1}H-NMR(DMSO) spectrum data of complex (2) reveal δ:6.5-7.7 (m , 8H , Ar-H) , (9.5,5.4)(m , 2H , OH), 3.4,3,7(d,2H,CH=CH) . The^{13}C-NMR(DMSO) spectrum data of derivative (2) display δ:196 (C7) , 175(C16) ,130 (C4,C11) ,127(C14) , 115-125(C-ar).

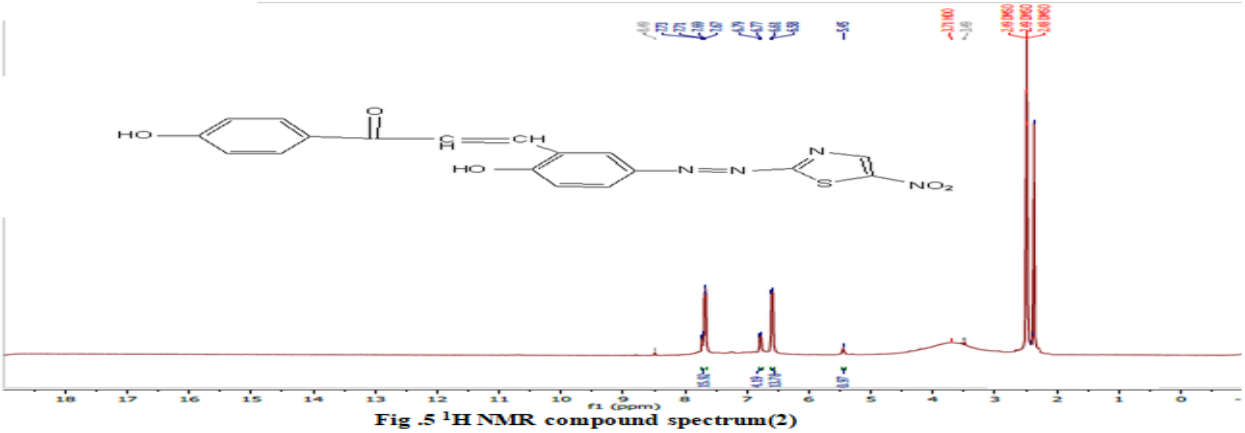


Fig .5 ^{1}H NMR compound spectrum(2)

***2-(3-(4-hydroxyphenyl)-4,5-dihydro-1H-pyrazol-5-yl)-4-((5-nitrothiazol-2-yl)diazenyl)phenol compound* (3)**

The infrared spectrum data of derivative (3) reveal absorption at (1455) cm^{-1}(-N=N-),(3304) cm^{-1} (OH) for phenol,and display band at (3189) for (N-H)for imidazol.The^{1}H-NMR(DMSO) spectrum data of complex (3) denote δ:6.9-8.9(m , 9H , Ar-H) , 10.1,5.9 (S , ٢H , OH) 10.6(s,1H,NH), 1.8(d,2H,CH_2), 2.9(t,1H,CH) . The^{13}C-NMR(DMSO) spectrum data reveal δ:160 (C16) , 145(C18) ,143 (C4,C11) ,136(C7) ,134(C12) 117-129(C-ar).

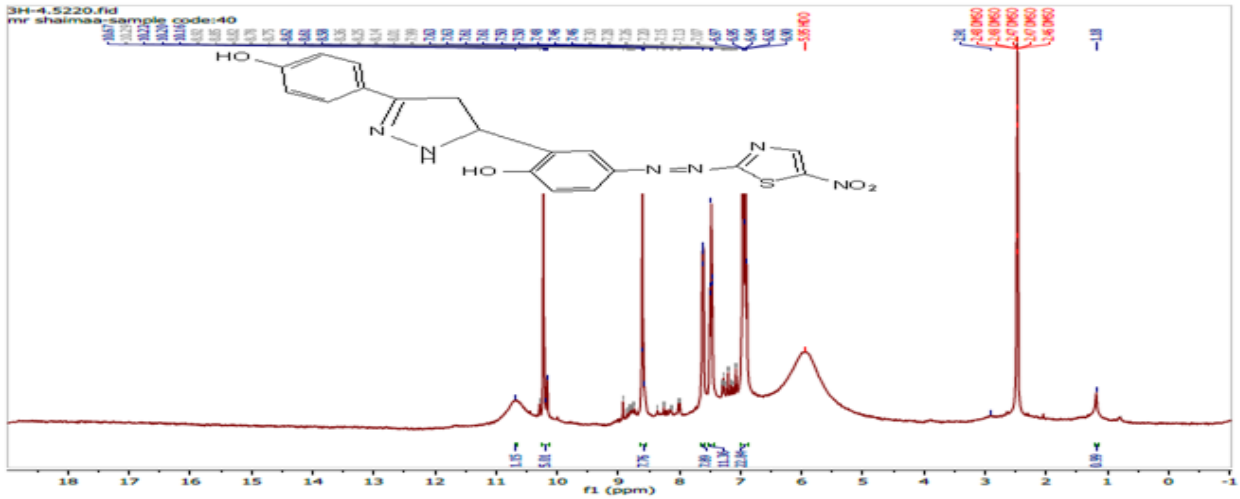


Fig .8 ^{1}H NMR spectrum of compound (3)

***2-(3-(4-hydroxyphenyl)-1-phenyl-4,5-dihydro-1H-pyrazol-5-yl)-4-((5-nitrothiazol-2-yl)diazenyl) phenol compound* (4)**

The infrared spectrum data of derivative (4) denote absorption at (1735) cm^{-1} for (C=O),(1458) cm^{-1}(-N=N-) ,(3409) cm^{-1} (OH) for phenol,and reveal band at (3139) for (N-H)for imidazol,and Vanishing band for NH_2 at (3379-3325)cm^{-1} .The^{1}H-NMR(DMSO) spectrum data of derivative (4) reveal δ:6.7-7.8(m , 14H , Ar-H) , 8.4,5.3 (S , 1H , OH) ,1.9 (d,2H,CH2) , 3.4(t,1H,CH). The^{13}C-NMR(DMSO) spectrum data display δ:164 (C16) , 24(C8) ,26(C9) , 115-144(C-ar).

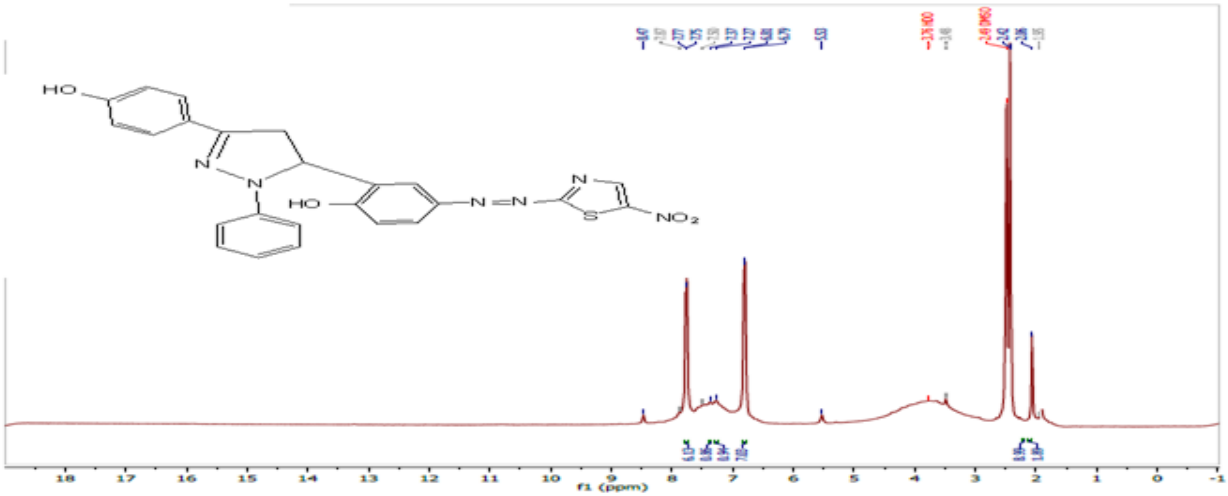


Fig .11 ^{1}H NMR compound spectrum (4)

***2-(1-(2,4-dinitrophenyl)-3-(4-hydroxyphenyl)-4,5-dihydro-1H-pyrazol-5-yl)-4-((5-nitrothiazol-2-yl)diazenyl)phenol compound* (5)**

The infrared spectrum data of derivative (5) reveal absorption at (1735) cm^{-1} for (C=O),(1458) cm^{-1}(-N=N-),(3409) cm^{-1} (OH) for phenol,and display band at (3139) for (N-H)for imidazol,and Vanishing band for NH_2 at (3379-3325)cm^{-1} .The^{1}H-NMR(DMSO) spectrum data of derivative (5) denote δ:6.8-8(m , 11H , Ar-H) , 8.4,4.4 (s , 2H , OH) ,1.7 (d , 2H,CH_2), 2.9 (t , `H,CH). The^{13}C-NMR(DMSO) spectrum data reveal δ:174 (C17) , 23(C8) ,25(C9) , 163(C19), 157(C7),134(C7),130(C9),115-129(C-ar).

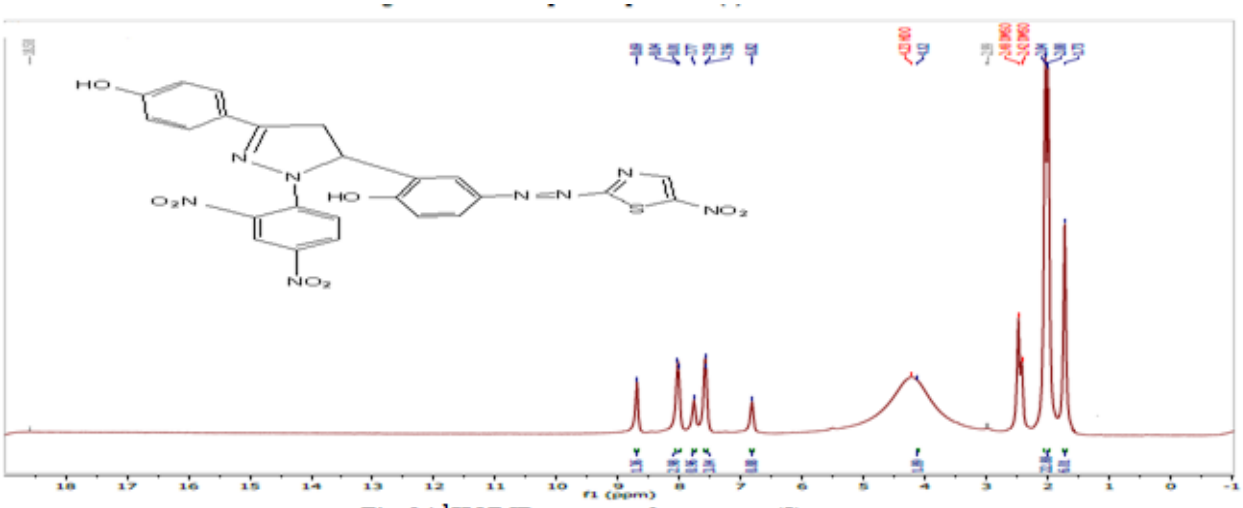


Fig .14 ^{1}H NMR compound spectrum (5)

Table (1) . The physical properties and analytical data of derivatives (1-11)

Compound	color	m.p °C	Yield%	R_f	Molecular formula (Mol.wt)	Found (calc.)% C	H	N
1	brown	200	78	0.4	$C_{10}H_6N_4O_4S$ (278.24)	(43.17) 43.23	(2.17) 2.20	(20.14) 20.01
2	brown	105	80	0.3	$C_{18}H_{12}N_4O_5S$ (396.38)	(54.54) 54.38	(3.05) 3.25	(14.13) 14.11
3	yellow	226	79	0.3	$C_{18}H_{14}N_6O_4S$ (410.41)	(52.68) 52.77	(3.44) 3.46	(20.48) 20.51
4	brown	131	73	0.3	$C_{24}H_{18}N_6O_4S$ (486.50)	(59.25) 59.59	(3.73) 3.29	(17.27) 17.42
5	yellow	126	77	0.3	$C_{24}H_{16}N_8O_8S$ (576.50)	(50.00) 50.21	(2.80) 2.38	(19.44) 19.53

Biological activity

1-Anti bacteria

Aftercare synthesized derivatives display important antibacterial action against to kind of bacteria *Escherichia coli* and *staphylococcus aurous* , the compounds that appeared very good activity are (5) against (staphylococcus aurous) on other hand, compound (5) display efficient action against (*staphylococcus aurous*), the outcomes of the antibacterial action were displayed in the table 2 shown the results of antibacterial

TABLE (2) . Reveal Biological action (anti bacteria) of derivatives (1-5).

Compounds No. Kind of bacteria

	E. coli	Staph. aureus
1	+	-
2	-	++
3	+	-
4	+	-
5	++	+++

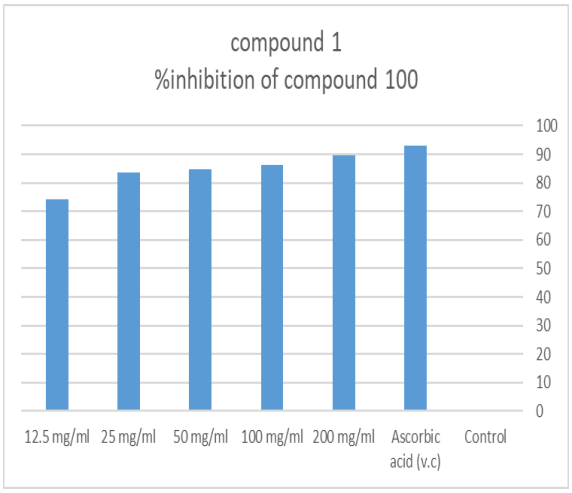
- The negative sambal (-) refer to No inhibition (inactive) but positive sambal (+) refer to (5-10) mm (slightly active) ,well (++) shamble refer to (11-20) mm (reasonably active) and (+++) sambal refer to (more than 20) mm (Good action).

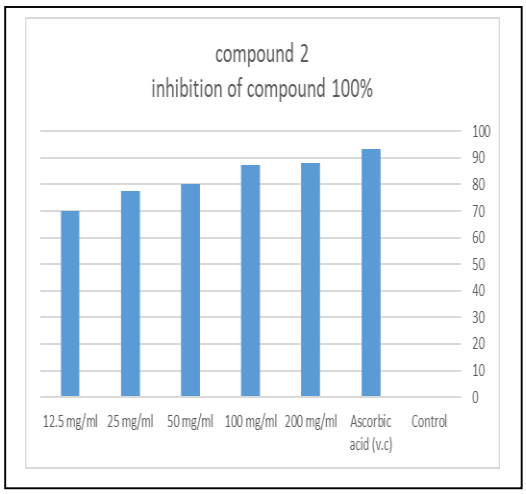
2- Antioxidant [9,10]

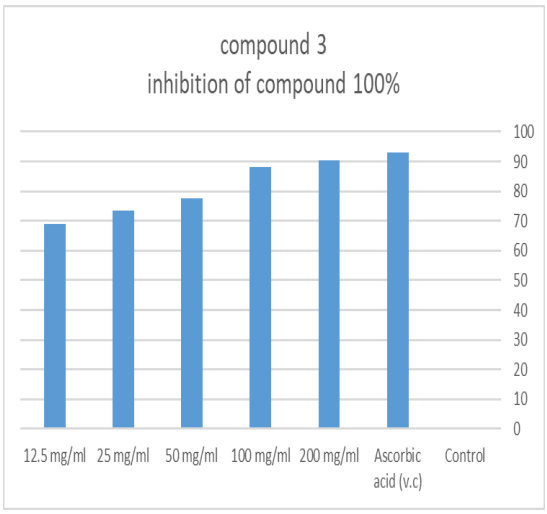
The compound 1,1-diphenyl-2-picrylhydrazyl (DPPH) is a stable free radical widely used to evaluate the antioxidant capacity of various substances. When an antioxidant interacts with a DPPH solution in ethanol, it donates a hydrogen atom to the radical, converting it into its non-radical form known as DPPH-H. This reaction is accompanied by a distinct color change from deep purple to pale yellow, which can be measured using a UV-Visible spectrophotometer. The decrease in absorbance at a wavelength of 517 nm reflects the sample's ability to scavenge free radicals.The compound (1) showed the best results ,Ascorbic acid showed the highest activity at 93.15%, serving as the reference standard.The tested sample demonstrated strong activity, especially at higher concentrations: At 200 mg/ml, the activity reached 89.47%, which is very close to that of ascorbic acid. As the concentration decreased, the activity gradually declined, indicating a dose-dependent relationship. At the lowest concentration (12.5 mg/ml), the activity dropped to 74.21%, showing a noticeable reduction in effect.

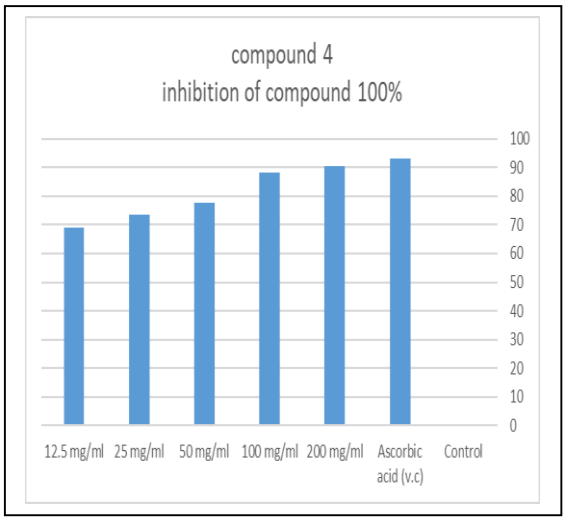
TABLE (3) . Reveal Biological action(anti oxidant) of derivatives (1-5).

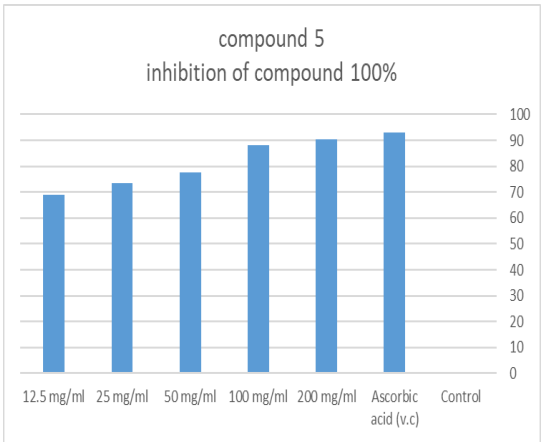
Con.	Inhibition percentage % comp.(1)	Inhibition percentage% comp.(2)	Inhibition percentage% comp.(3)	Inhibition percentage% comp.(4)	Inhibition percentage% comp.(5)
Control	0	0	0	0	0
Ascorbic acid (v.c)	93.15	93.15	93.15	93.15	93.15
200 mg/ml	89.47	88	90.33	90.33	90.33
100 mg/ml	86.31	87.1	88.12	88.12	88.12
50 mg/ml	84.73	80.3	77.69	77.69	77.69
25 mg/ml	83.68	77.4	73.55	73.55	73.55
12.5 mg/ml	74.21	70.11	68.91	68.91	68.91











Fig(6) inhibition of compound (1-5) as anti oxidant

Conclusions

The tested sample exhibits promising biological activity, particularly at higher concentrations, and could potentially serve as an alternative to ascorbic acid in certain applications. The results suggest a clear concentration-effect relationship, supporting the idea that controlled dosing can achieve desired efficacy.

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