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Click synthesis, anti-bacterial activity, and molecular docking study of a new Benzocaine derivatives

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ABSTRACT

This study included synthesis of new Benzocaine derivatives (**B2-B16**) synthesized by converting of Benzocaine into benzocaine hydrazide **B1** that cyclized into 1,3,4 oxadiazole 2-thion this compound cyclized into carbinol derivatives **B4**. The **B4** compound esterified with various bioactive carboxylic acids to generate (**B6-B16**) derivatives. The newly synthesized compounds were confirmed by available spectral methods: FT-IR, ¹H-NMR. The antibacterial activity for synthesized compounds was evaluated against two pathogenic bacteria, *A.baumannii* and *S.aureus*. all the compounds demonstrated promising activity against *S.aureus* except **B8** while **B5,B6, B12** and **B13** showed moderate activity against of *A.baumannii* . Molecular modeling studies were performed for the compounds that exhibited high antibacterial activity against the binding sites of biotin protein ligase (PDB:ID: **4dq2**) and compound with ATP phosphoribosyltransferase (PDB:ID:**8oy0**) the obtained results indicated to a good binding mods with targetuxed protein.uhm

Keywords: Antibacterial, Benzocaine, molecular docking, Triazole

1. Introduction

Fungal and bacterial diseases represent a major challenge to human, animal, and plant health[1], posing significant threats to public well-being, agricultural productivity, and the global economy[2]. Fungal pathogens are capable of invading living tissues and producing harmful toxins, which can lead to crop deterioration, reduced nutritional quality, and in severe cases[3], chronic dermatological and respiratory conditions in humans[4]. Similarly, pathogenic bacteria are responsible for a wide range of infectious and contagious diseases affecting humans and animals, while also causing devastating damage to agricultural systems by infecting crops[5].

2. Materials and Methods

All chemicals and solvents were of analytical grade and used without further purification supplied by (sigma Aldrich) Himedia Merck alfa Aesar.

Melting points were measured by open glass capillary method on a Stuart SMP 10. IR spectra were recorded on a Shimadzu FT-IR-8400S spectrophotometer using KBr pellets. The ¹H-NMR spectra were

measured in d^6 -DMSO by using a Varian 500 MHz- a vance III NMR. The biological activities were screened against three bacterial strains (proteus infection),(Staphylococcus aureus) and (Escherichia coli) using mueller-hinton agar medium sterilized at 121 °C under high pressure, an incubator.

2.1.Synthesis of Naproxen ethyl ester (L₁) [11]

Naproxen (4.6gm, 0.02 mol) was dissolved in (40 ml) of absolute ethanol with stirring and H₂SO₄ 98% (2ml) was added dropwise while stirring continuously. Under reflux the mixture was heated for (8 hours). then cooled and neutralized by 10%NaHCO₃.After that, filtered, washed with water, dried and recrystallized from absolute ethanol . Yield=87%.

2.2. Synthesis Naproxen hydrazide (L₂) [12]

In a 100 mL round-bottom flask (5.16 gm/0.02 mol) of Naproxen ethyl ester was dissolved in (10 mL)of hydrazine hydrate 80% and (10 mL)of pure ethanol and the mixture was refluxed for(8 hours). The liquid was cooled and then poured onto crushed ice,filtered, rinsed with water ,dried and recrystallized from absolute ethanol.

Yield=98%.

2.3. Synthesis p-nitro acetanilide (L₃) [13]

In a round-bottomed flask (2.5gm)of acetanilide was added in(2.5ml) of glacial acetic acid and mixed in a magnet mixer to dissolve it. After that, (10 ml) of (H₂SO₄) was added and it was heated until it completely dissolved. The flask was placed in an ice bath and cooled to 5°C. The nitration mixture was prepared of (1 ml) of concentrated HNO₃ and (0.7 ml) of concentrated H₂SO₄. then cooled to 5°C and progressively added to the acetanilide solution. After completing the addition, the mixture rested for (30 minutes)at room temperature and was poured to (50 ml) of cold water to obtain a crude precipitate .Then filtered, washed with water, dried and recrystallized with absolute ethanol. Yield=91%.

2.4. Synthesis of chalcones derivatives (L₄-L₈)[14]

Para-nitroacetanilide(L₃) (0.54gm/0.003mol) was dissolved with (0.003mol) of aromatic aldehydes in 96% ethanol. Then, (0.8gm) of NaOH was dissolved in (10 ml) of distilled water and (8 ml) of absolute ethanol. It was added to the mixture and stirred for (5 hours). Then the mixture was neutralized with a dilute solution of HCl, where a precipitate was formed. Then filtered, dried and recrystallized from absolute ethanol. Yield= 79%

3-[4-(dimethylamino)phenyl]-N-(4-nitrophenyl)prop-2-enamide (L₄):

Red powder, Yield =83%, m.p=165-167°C, IR(cm⁻¹, KBr): 1645(C=O), 1587(C=C alkene), 3041(C-H aromatic), 1512(C=C aromatic), 2686(C=H aliphatic).

N-(4-nitrophenyl)-3-phenylprop-2-enamide (L₅):

Yellow powder, Yield =61%, m.p=170-172°C, IR(cm⁻¹, KBr): 1681(C=O), 1599(C=C alkene), 3159(C-H aromatic), 1504(C=C aromatic), 3093(C=H aliphatic).

3-(4-bromophenyl)-N-(4-nitrophenyl)prop-2-enamide (L₆):

Yellow powder, Yield =69%, m.p=87-89°C, IR(cm⁻¹, KBr): 1633(C=O), 1599(C=C alkene), 3084(C-H aromatic), 1502(C=C aromatic), 2905(C=H aliphatic). N,3-bis(4-nitrophenyl)prop-2-enamide (L₇):Orange powder, Yield =71%, m.p=157-159°C, IR(cm⁻¹, KBr): 1650(C=O), 1548(C=C alkene), 3062(C-H aromatic), 1503(C=C aromatic), 2980(C=H aliphatic).

3-(4-chlorophenyl)-N-(4-nitrophenyl)prop-2-enamide (L₈):

Yellow powder, Yield =88%, m.p=159-160°C, IR(cm⁻¹, KBr): 1681(C=O), 1581(C=C alkene), 3093(C-H aromatic), 1506(C=C aromatic), 2821(C-H aliphatic).

2.5. Synthesis of pyrazolines derivatives (L₉-L₁₃) [15]

In around-bottomed flask(0.002mol) of Chalcones was dissolved with (0.48gm/0.002mol) naproxen hydrazide and (0.08gm) of NaOH in (20ml) of absolute ethanol. The mixture was stirred and refluxed for (8-12 hours). The precipitate was filtered, washed with distilled water, dried, and recrystallized with absolute ethanol.

Yield= 81%

1-{3-[4-(dimethylamino)phenyl]-5-[(4-nitrophenyl)amino]-4,5-dihydro-1H-pyrazol-1-yl}-2-(6-methoxynaphthalen-2-yl)propan-1-one (L₉):

Yellow powder, Yield = 80%, m.p=248-250°C, IR(cm⁻¹, KBr): 3188(N-H acetanilide) 2995(C-H aromatic), 2935-2902(C-H aliphatic) 1651(C=O), 1606(C=N), 1525-1483(C=Caromatic). ¹H-NMR(500MHz,dmsO)δ(ppm):1.35(s,6 H,CH₃);2.8(s,3H,CH₃O); 3.9(d,2H,CH₂); 4.01(t,1H,CH); 6.9-8.24(p,14H,Ar-H); 11.4(s,1H,NH).

1-[3-(4-bromophenyl)-5-[(4-nitrophenyl)amino]-4,5-dihydro-1H-pyrazol-1-yl]-2-(6-methoxynaphthalen-2-yl)propan-1-one (L₁₀):

White powder, Yield = 91%, m.p= 200-202°C, IR(cm⁻¹, KBr): 3190(N-H acetanilide) 3018(C-H aromatic), 2978-2904(C-H aliphatic) 1660(C=O), 1604(C=N), 1514-1485(C=Caromatic), 854(C-Br). ¹H-NMR(500MHz,dmsO)δ(pp m):1.5(s,3H,CH₃);3.42(s,3H, CH₃O); 3.9(d,2H, CH₂); 4.91(t,1H, CH); 7.1-9.3(p,14H, Ar-H); 11.5(s,1H, NH).

2-(6-methoxynaphthalen-2-yl)-1-{5-[(4-nitrophenyl)amino]-3-phenyl-4,5-dihydro-1H-pyrazol-1-yl}propan-1-one (L₁₁):

Yellow powder, Yield = 70%, m.p= 190-192°C, IR(cm⁻¹, KBr): 3186(N-H acetanilide) 3003(C-H aromatic), 2970-2933(C-H aliphatic) 1662(C=O), 1577(C=N), 1514-1487(C=Caromatic). ¹H-NMR(500MHz,dmsO)δ(ppm):1.94(s,3 H,CH₃);2.5(s,3H, CH₃O); 3.98(d,2H, CH₂); 4.82(t,1H, CH); 6.8-8.12(p,15H, Ar-H); 11.5(s,1H, NH).

2-(6-methoxynaphthalen-2-yl)-1-[3-(4-nitrophenyl)-5-[(4-nitrophenyl)amino]-4,5-dihydro-1H-pyrazol-1-yl]propan-1-one (L₁₂):

Yellow powder, Yield = 95%, m.p= 212-214°C, IR(cm⁻¹, KBr): 3186(N-H acetanilide) 3001(C-H aromatic), 2972-2933(C-H aliphatic) 1662(C=O), 1604(C=N), 1514-1485(C=Caromatic), 885(C-NO₂). ¹H-NMR(500MHz,dmsO)δ(p pm):1.52(s,3H,CH₃);2.59(s,3H,CH₃O); 3.85(d,2H, CH₂); 4.92(t,1H, CH); 7.5-8.5(p,14H, Ar-H); 11.92(s,1H, NH).

1-[3-(4-chlorophenyl)-5-[(4-nitrophenyl)amino]-4,5-dihydro-1H-pyrazol-1-yl]-2-(6-methoxynaphthalen-2-yl)propan-1-one (L₁₃):

Yellow powder, Yield = 87%, m.p= 188-190°C, IR(cm⁻¹, KBr): 3354(N-H acetanilide) 3095(C-H aromatic), 2929-2930(C-H aliphatic) 1681(C=O), 1597(C=N), 1502-1402(C=C aromatic), 821(C-Cl). ¹H-NMR(500MHz,dmsO)δ(ppm):1.59(s,3H,CH₃);2.29(s,3H,CH₃O);3.92(d,2H, CH₂); 4.15(t,1H,CH);7.69-8.43(p,14H, Ar-H); 10.59(s,1H, NH).

3. Results and discussion

3.1.chemistry:

Chalcones were prepared by the Schmidt-Claisen condensation reaction of para-nitrostanalide with aromatic aldehydes, Naproxen ethyl ester (L₁) was prepared by dissolving it in ethanol and concentrated H₂SO₄, and the ester was converted to naproxen hydrazide (L₂) via hydrazine hydrate. Pyrazolines(L₉-L₁₀) were prepared by the reaction of chalcones(L₄-L₈) with naproxen hydrazide in the presence of ethanol as shown in the following schemes shown in the following scheme:

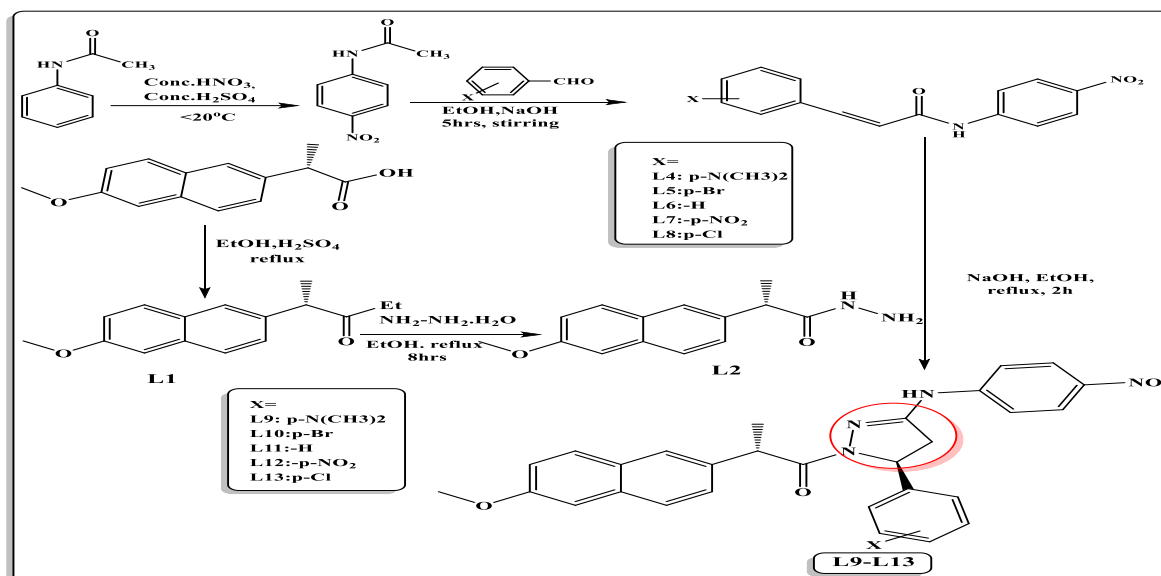


Fig. 1 Synthesis of pyrazolines (L₉-L₁₃)

The new pyrazoline derivatives were measured by infrared spectroscopy (IR) by absence of NH₂ in the region between 3250-3300 cm⁻¹, and C=O appeared for the compounds in the range (1651-1681)cm⁻¹, a stretching band also appeared at the frequency (1577-1606) cm⁻¹ indicating the group (C=N).

The ¹H-NMR spectrum of pyrazoline derivatives (L₉-L₁₃) showed a triple signal at (4.5-4.9)ppm indicating a (CH) proton and a double signal appeared at (3.4-3.9) ppm indicating a (CH₂) protons at position 5 in the pyrazoline ring.

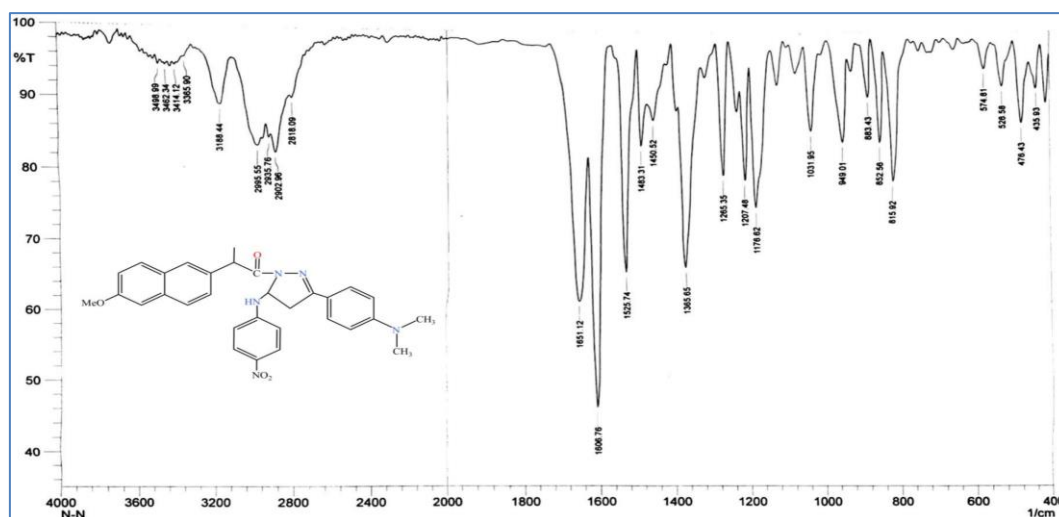


Fig. 2. FT-IR Spectrum of (L₉) derivative

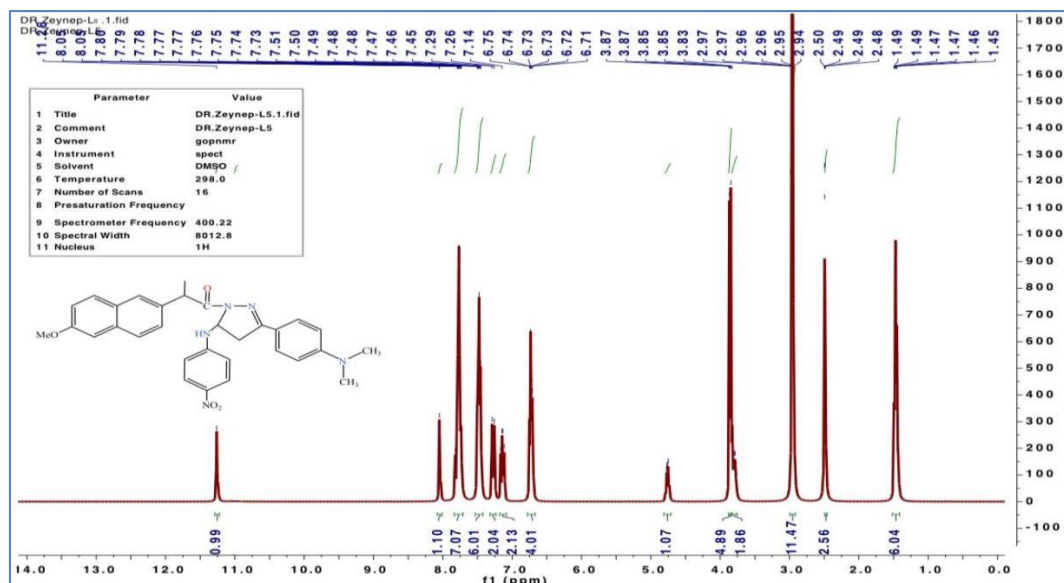


Fig. 3. ¹H-NMR Spectrum of (L₉) derivative

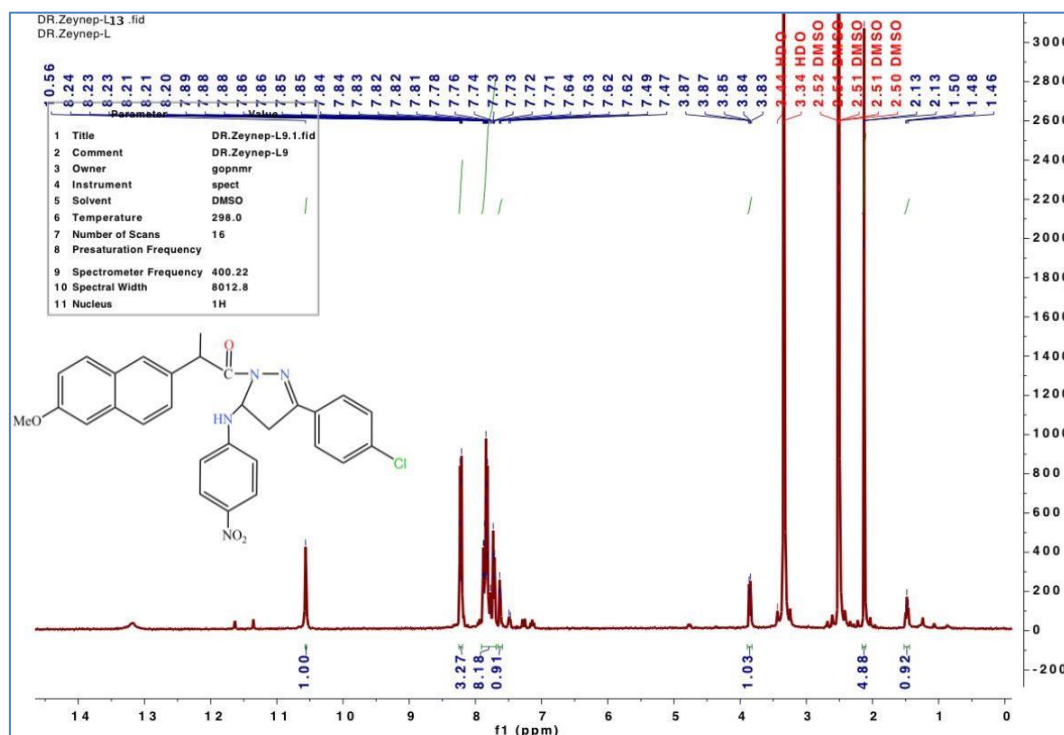


Fig. 3. ¹H-NMR Spectrum of (L₉) derivative

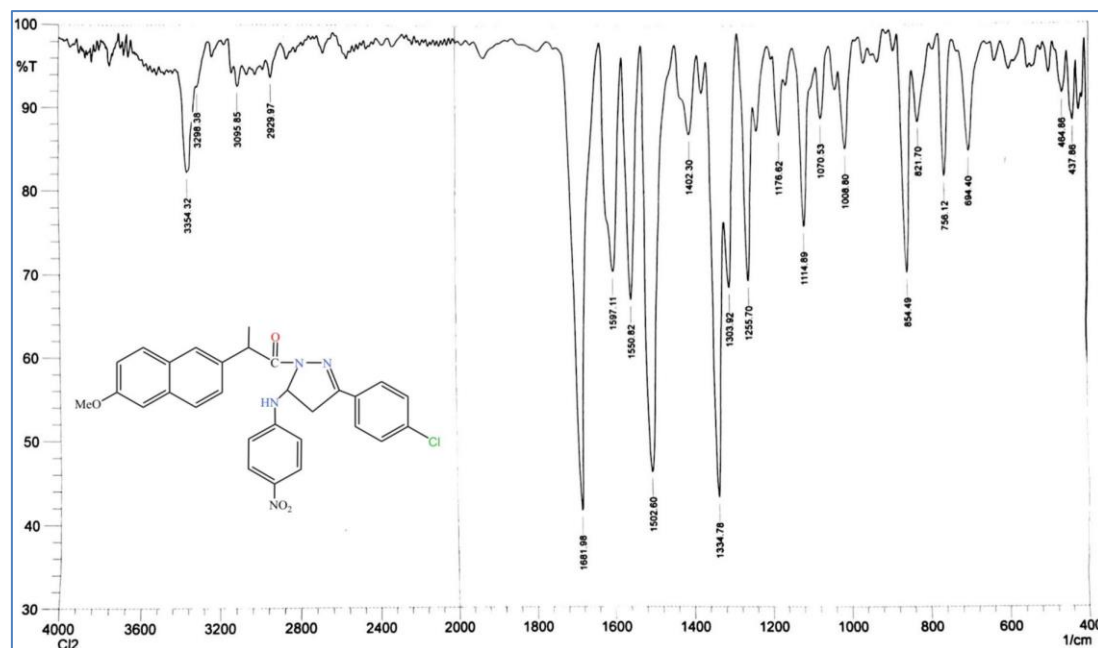


Fig. 5. ¹H-NMR Spectrum of (L₁₃)

3.2. Biological parts

The antibacterial activity of the prepared compounds was evaluated against several types of bacteria which are (*Proteus infection*, *Staphylococcus aureus* and *Escherichia coli*) as shown in Fig (5)(6) and (7). Where one method was tested in testing the effectiveness of the prepared compounds, which is the diffusion method in the holes (Agar-well diffusion method). After that, the culture medium was inoculated with bacterial isolates, the results were read after 24 hours and the compounds showed antibacterial activity as the microbial diameter (inhibition zones) ranged from (5 to 30) mm and was compared to the inhibitory diameter of standard antibiotics such as ciprofloxacin and norfloxacin.

This indicates that these solutions have varying effectiveness according to their concentrations as shown in the table below:

Table 1. antibacterial activity of pyrazolines derivatives

Comp. No	Conc. mg/ml.	Zone of inhibition (mm)		
		Staph. aureus	E.coli	proteus
L ₉	0.01	15	-	13
	0.001	7	-	15
	0.0001	12	-	20
L ₁₀	0.01	-	-	-
	0.001	-	-	-
	0.0001	-	-	-
L ₁₁	0.01	-	7	5
	0.001	-	13	17
	0.0001	-	10	8
L ₁₂	0.01	12	13	10
	0.001	20	15	8

L13	0.0001	5	9	15
Ciprofloxacin	0.01	-	-	14
	0.001	-	-	12
	0.0001	-	-	17
	0.001	12	12	12
Norfloxacin	0.001	11	11	11

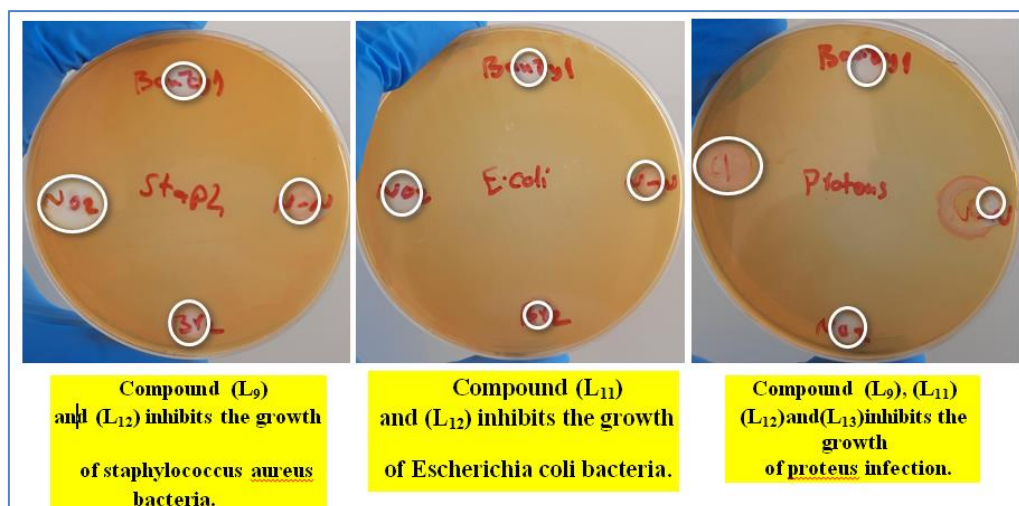


Fig. 6. results of antibacterial activity of new Naproxen-pyrazoline derivatives

Molecular docking protocol:

This study includes molecular modeling study; this term indicates designing the candidate lead compound by computer software. Molecular docking studies were investigated via employing Auto Dock vina programs. The **biotin protein ligase** enzyme (PDB:ID=4dq2), **biotin carboxylase**(PDB:ID: 3jzf), **N-acetylneuraminate lyase** (PDB:ID=6h4e), was abstracted from RCSB, PDB (Protein Data Bank) site. The ligand was prepared by minimizing of energy through MMFF94 tool. In regarding enzyme, water molecules were removed and polar hydrogens were added as well as Kollman charge this process were performed by Auto Dock tool 1.5.6 program. The 2D,3D binding mods of ligand were visualized by Discovery Studio 2020 Client [16].

Molecular docking study:

Molecular docking results that resulted in this computational simulation indicated that the **L11** compound interact with biotin carboxylase(PDB:ID: 3jzf) at docking score -8.0 kcal/mol with RMSD value 2.164, 3.620Å, 2D and 3D screened visualized images exhibited presence two hydrogen bonds : (ASN:B:88) with NO₂ group at para position (LYS:B:116) with carbonyl group as well as other interactions that compares: Pi-Pi Stacked, Pi-Pi T-shaped, Amide-Pi Stacked as illustrated in fig(5), table (2):

the **L12** compound interact with biotin carboxylase(PDB:ID: 3jzf) at docking score -8.3 kcal/mol with RMSD value 3.498, 6.983Å, 2D and 3D screened visualized images exhibited presence two hydrogen bonds : (ASN:B:88) with NO₂ group at para position (LYS:B:116) with carbonyl group as well as other interactions that compares: Pi-Pi Stacked, Pi-Pi T-shaped, Amide-Pi Stacked interactions, as illustrated in fig(5), table (2):

the **L9** compound interact with N-acetylneuraminate lyase (PDB:ID=6h4e) at docking score -7.5 kcal/mol with RMSD value 4.930, 9.745Å, 2D and 3D screened visualized images exhibited presence four hydrogen bonds: (THR:A:47), (ASN:A:168), (LYS:A:166) (SER:A:210) with NO₂ group at para position

(LYS:B:116) with carbonyl group as well as other interactions that compares: pi-sigma, pi-anion, pi-cation, pi – alkyl, alkyl interactions , as illustrated in fig(5), table (2):

the **L12** compound interact with N-acetylneuraminate lyase (**PDB:ID=6h4e**) at docking score

-7.7 *kcal/mol* with RMSD value 5.378, 10.173 Å°, 2D and 3D screened visualized images exhibited presence two hydrogen bonds : (ASN:A:168), (SER:A:210) with NO₂ group at para position as well as other interactions that compares: pi-sigma, pi-ca Pi-Sulfur, Pi-Pi Stacked interactions , as illustrated in fig(5), table (2):

the **L13** compound interact with N-acetylneuraminate lyase (**PDB:ID=6h4e**) at docking score

-7.5s *kcal/mol* with RMSD value 5.477, 9.028Å°, 2D and 3D screened visualized images exhibited presence two hydrogen bonds : (THR:A:47), (ASN:A:168), (LYS:A:166) (SER:A:210) with NO₂ group at para (SER:A:210) with OCH₃ group, GLU:A:144 with NH group as well as other interactions that compares: pi- stacked , pi-alkyl , alkyl interactions , as illustrated in fig(5), table (2):

the **L9** compound interact with N-acetylneuraminate lyase (**PDB:ID=6h4e**) at docking score -8.2 *kcal/mol* with RMSD value 13.903, 17.188 Å°, 2D and 3D screened visualized images exhibited presence two hydrogen bonds : (ASN:A:154), (SER:A:151) with NH group, group as well as other interactions that compares: Pi-Pi Stacked, Pi-Pi T-shaped, Amide-Pi Stacked pi-alkyl , alkyl interactions, as illustrated in fig(5), table (2):

the **L12** compound interact with N-acetylneuraminate lyase (**PDB:ID=6h4e**) at docking score

-6.9 *kcal/mol* with RMSD value 4.410, 6.632 Å°, 2D and 3D screened visualized images exhibited presence two hydrogen bonds : (SER:A:93) with NO₂ group at para position, (GLU:A:194) with NH group as well as other interactions that compares: pi-sigma, pi-anion, pi-cation, Pi-Pi Stacked, Alkyl, pi-alkyl interactions , as illustrated in fig(5), table (2):

Table 2. Molecular docking result of the synthesized compound with binding site of of lactate dehydrogenase enzyme(PDB:ID: 4i8x)

Comp No.		Affinity (Kcal/mol)	RMSD l.b. (Å°)	RMSD u.b. (Å°)	Distance (Å°)	Main residue	Type of Interaction
L11	3jzf	-8.0	2.164	3.620	3.39755	B:ASN290:ND 2 - :UNK1:O	Conventional Hydrogen Bond
					3.33751	B:GLN294:NE 2 - :UNK1:O	Conventional Hydrogen Bond
					4.65903	:UNK1 - :UNK1	Pi-Pi Stacked
					3.90053	:UNK1 - :UNK1	Pi-Pi Stacked
					4.839	B:HIS209 - :UNK1	Pi-Pi T-shaped
					3.71373	B:GLY165:C, O;GLY166:N - :UNK1	Amide-Pi Stacked
					4.40155	B:PHE84 -	Pi-Alkyl

						:UNK1:C	
L12	3jzf	-8.3	3.498	6.983	3.39755	:UNK-:UNK1	Conventional Hydrogen Bond
					3.33751	:UNK1 :UNK1	Conventional Hydrogen Bond
					4.65903	B:HIS209:UNK1	Pi-Pi Stacked
					3.90053	B:GLY165:C, O;GLY166:N - :UNK1	Pi-Pi Stacked
					4.839	B:PHE84 - :UNK1:C	Pi-Pi T-shaped
					3.71373	:UNK1 -:UNK1	Amide-Pi Stacked
					4.40155	:UNK1 - :UNK1	Pi-Alkyl
L9	6h4e	-7.7	5.378	10.173	2.35814	A:ASN168:HD21 - :UNK1:O	Conventional Hydrogen Bond
					1.90062	A:SER210:HN :UNK1:O	Conventional Hydrogen Bond
					3.79102	A:GLY209:CA- :UNK1:O	Carbon Hydrogen Bond
					3.69182	A:LEU275:CD 2 - :UNK1	Pi-Sigma
					5.76124	A:MET141:SD - :UNK1	Pi-Sulfur
					4.732	:UNK1 -:UNK1	Pi-Pi Stacked
					3.89995	:UNK1 - :UNK1	Pi-Pi Stacked
					4.32893	:UNK1:C - A:PRO170	Alkyl
L12	6h4e	-7.5	5.477	9.028	2.53777	A:THR140:H N - :UNK1:O	Conventional Hydrogen Bond
					2.79779	A:MET141:H N - :UNK1:O	Carbon Hydrogen Bond
					2.4571	A:ASN168:H D22 - :UNK1:O	Pi-Sigma
					2.52966	A:SER210:HN - :UNK1:O	Pi-Sulfur

					2.16376	:UNK1:H - A:GLU194:OE 2	Pi-Pi Stacked
					3.34833	A:GLY209:CA:UNK1:O	Pi-Pi Stacked
					4.85962	:UNK1 :UNK1	Alkyl
					3.73417	UNK1 :UNK1	Alkyl
L13	6h4e	-7.5	5.477	9.028	2.53777	A:THR140:H N - :UNK1:O	Conventional Hydrogen Bond
					2.79779	A:MET141:H N - :UNK1:O	Conventional Hydrogen Bond
					2.4571	A:ASN168:H D22 :UNK1:O	Conventional Hydrogen Bond
					2.52966	A:SER210:HN :UNK1:O	Conventional Hydrogen Bond
					2.16376	:UNK1:H - A:GLU194:OE 2	Conventional Hydrogen Bond
					3.34833	A:GLY209:CA- :UNK1:O	Carbon Hydrogen Bond
					4.85962	:UNK1 - :UNK1	Pi-Pi Stacked
					3.73417	:UNK1 - :UNK1	Pi-Pi Stacked
					4.14376	A:ALA10 - :UNK1:C	Alkyl
					5.47583	:UNK1 - A:ILE245	Pi-Alkyl
L9	4dq2	-8.2	13.90 3	17.188	3.39222	A:ASN154:N D2 - :UNK1:O	Conventional Hydrogen Bond
					2.08388	:UNK1:H - A:SER151:OG	Conventional Hydrogen Bond
					3.64768	A:THR193:CB :UNK1:O	Carbon Hydrogen Bond
					3.68624	:UNK1:C - A:MET195:O	Carbon Hydrogen Bond
					3.79635	A:SER151:OG	Pi-Donor

						- :UNK1	Hydrogen Bond
					3.62333	A:TYR303:O H - :UNK1	Pi-Donor Hydrogen Bond
					3.98908	A:SER148:CB - :UNK1	Pi-Sigma
					3.49978	A:MET195:CE - :UNK1	Pi-Sigma
					4.92506	A:ILE150:C,O ;SER151:N - :UNK1	Amide-Pi Stacked
					4.26217	:UNK1:C - A:LYS152	Alkyl
L12	4dq2	-6.9	4.410	6.632	3.25704	A:SER93:OG - :UNK1:O	Conventional Hydrogen Bond
					2.61624	:UNK1:H - A:GLU194:OE 2	Conventional Hydrogen Bond
					4.5157	A:LYS99:NZ - :UNK1	Pi-Cation
					3.95438	A:LEU192:CD 1 - :UNK1	Pi-Sigma
					4.7221	:UNK1 - :UNK1	Pi-Pi Stacked
					3.76373	:UNK1 - :UNK1	Pi-Pi Stacked
					4.57427	:UNK1:C - A:MET195	Alkyl
					4.36071	:UNK1 - A:ARG120	Pi-Alkyl

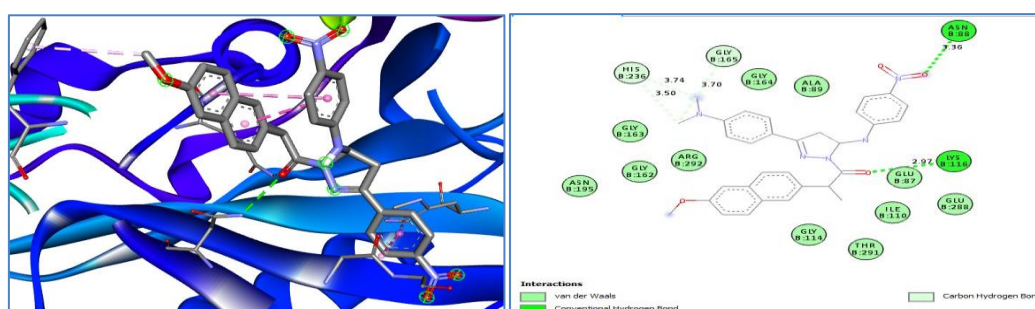


Fig. 7. The interaction between L11 compound with binding site of biotin carboxylase enzyme (PDB:ID: 3jzf) in 3D and 2D dimensions.

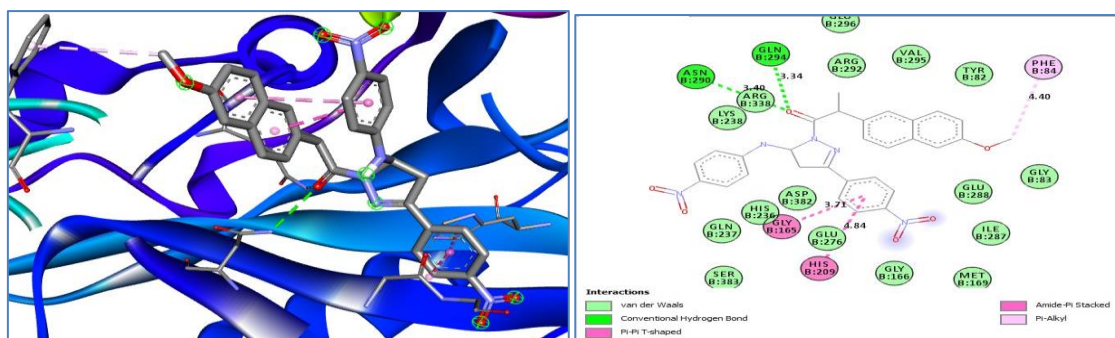


Fig. 8. The interaction between L12 compound with binding site of biotin carboxylase enzyme (PDB:ID: 3jzf) in 3D and 2D dimensions.

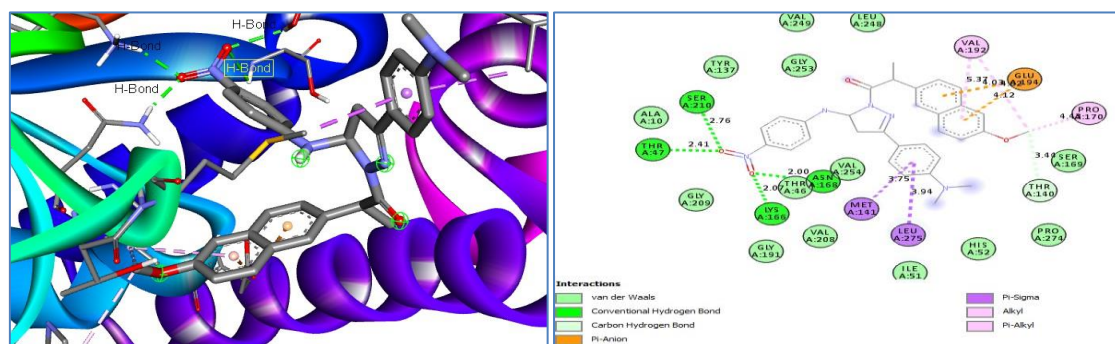


Fig. 9. The interaction between L9 with binding site of N-acetylneuraminate lyase (PDB:ID=6h4e), in 3D and 2D dimensions.

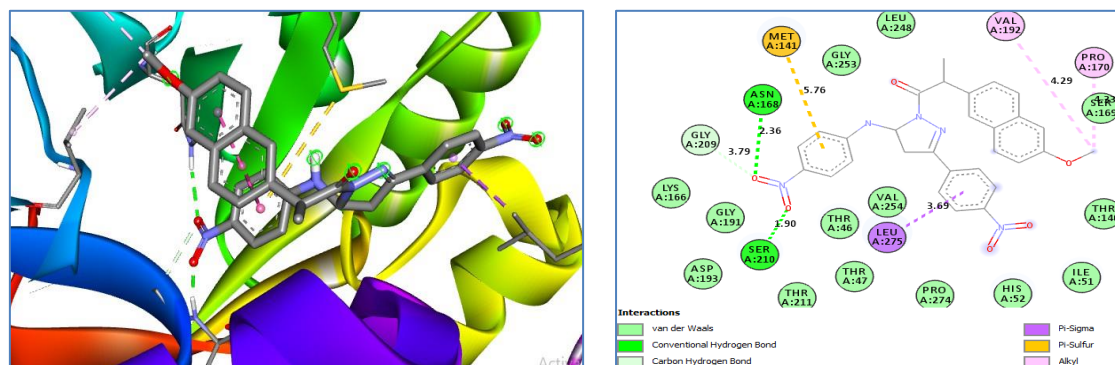


Fig. 10. The interaction between L12 with binding site of N-acetylneuraminate lyase (PDB:ID=6h4e), in 3D and 2D dimensions.

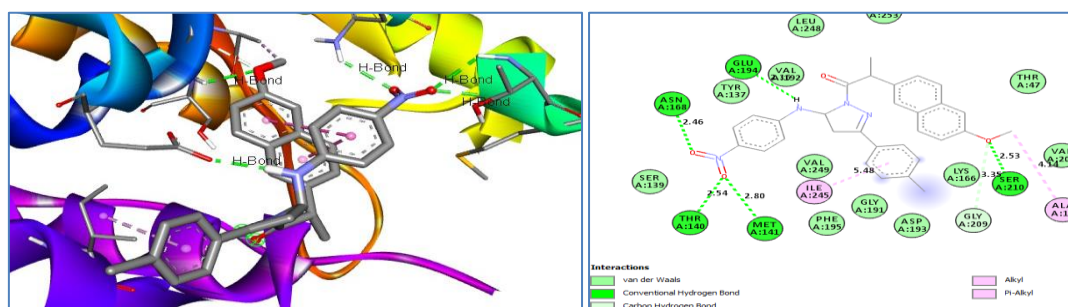


Fig. 11. The interaction between L13 with binding site of N-acetylneuraminate lyase (PDB:ID=6h4e), in 3D and 2D dimensions.

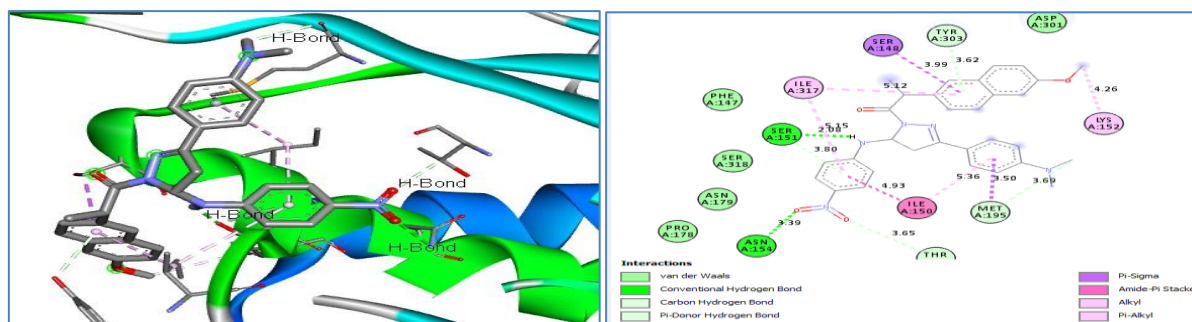


Fig. 12. The interaction between L9 with binding site of biotin protein ligase enzyme (PDB:ID=4dq2), in 3D and 2D dimensions.

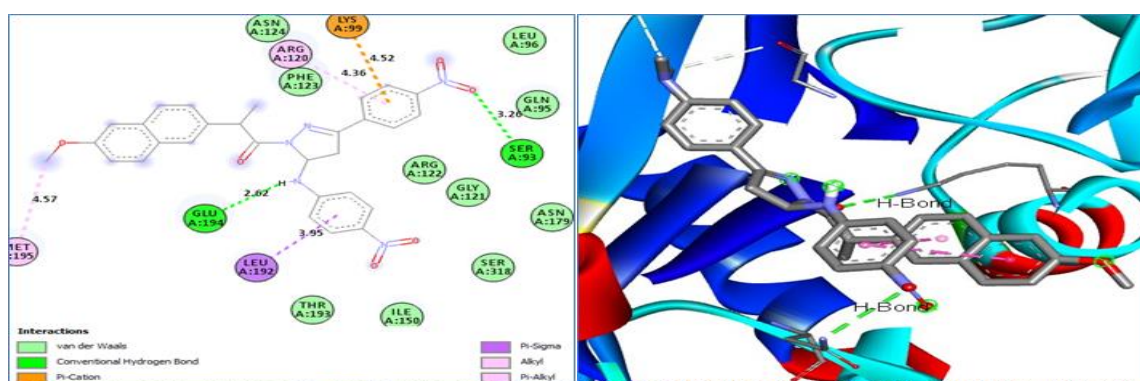


Fig. 13. The interaction between L12 with binding site of biotin protein ligase enzyme (PDB:ID=4dq2), in 3D and 2D dimensions.

Conclusion

New pyrazolines (**L9-L13**) were prepared from the reaction of chalcones with naproxen hydrazide and these compounds were characterized by FT-IR and H-NMR and showed biological activity against 3 types of pathogenic bacteria *E.coli*, proteus and staph. We conclude that the pyrazoline nucleus is one of the basic pharmaceutical preparations for the design development of new drugs.

Author Contributions

All authors mentioned above must have made a significant contribution to the work Zainab F. Saadallah designed the study; conducted experiments Fadhil Dawood analyzed the data, wrote the manuscript... etc.

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The authors declare no competing interests

Ethical Approval and Consent

Not Applicable

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