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Synthesis, Characterization and Biological activity study for new hybrid polymers by grafting 1,3,4-triazole and 1,2,4-oxadiazle moieties onto polyvinyl chloride

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Abstract

In this work 1,2,4-Triazole and 1,3,4-Oxadiazole derivatives were synthesized from [4-(4-hydroxy-3-methyl naphthyl) diazenyl] benzoic acid [M1], which were converted to [4-(4-hydroxy-3-methyl naphthyl)diazenyl] benzoate [M2]. Benzoate derivative reacted with hydrazine afforded [M3] which cyclized by carbon disulfide to give compound [M4]. In addition, cyclization of compound [M3] was accomplished by sodium hydroxide and thiosemicarbazide to give triazole- thiol [M5]. Hybrid polymers [M6 and M7] were synthesized by grafted 1,3,4-oxadiazole [M4], and 1,2,4-triazole [M5] onto the polyvinyl chloride in the presence of pyridine and tetrahydrofuran. These compounds were characterized by the following techniques: FT-IR, and ^{1}H, ^{13}C NMR spectroscopies, and elemental analysis C,H,N,S. The biological activity study, IC_{50} value was significantly decreased in M6 (IC_{50}=25.76 µM/ml) and M7 (IC_{50}=21.41 µM/ml). In addition, the biological activity for final products achieved with good results.

Keywords: 2-Methyl-1-Naphthol, Azo dyes, 1,3,4-Oxadiazole, 1,2,4-triazole, PVC, cytotoxicity, anti-bacterial

1.Introduction

Azo dyes have distinctive biological applications such as antineoplastic, antidiabetics, cleaning agents, anti-inflammatory and other accessible chemotherapeutic agents. Azo compounds are exceedingly colored and utilized as dyes and pigments for a long time, as well as, Azo colors have extraordinary significance concurring their environmental stability, electrical and optical properties [1-3].

Heterocyclic compound membered rings have involved an imperative put within the pharmaceuticals and industrial field. 1,3,4-oxadiazoles are vital heterocyclic compounds which considered as a part in synthesis of drugs, polymers, and dyes [4-6].

In expansion, they have wide applications in agriculture and medicine [7]. Mercapto and thione substituted derivatives of 1,2,4-triazole compounds have been utilized in completely different applications such as biological activity. Also, 1,2,4-triazole have a great satiability to acidic-basic hydrolysis and oxidative-reductive conditions [8,9].

The Heterocyclic compounds specialy five-member heterocyclic compounds contain nitrogen as heteroatom, mainly triazoles ($C_2H_3N_3$) and their derivatives has important properties [10]. Five-membered nitrogen heterocyclic compounds are exceptionally crucial structural parts and considered as biologically active compounds [11-15]. They also play important role in production of pesticides,corrosion inhibitor, dyes, acid- base indicator, and other industrial chemicals [16-20]. Polyvinyl chloride (PVC) has important properties, hence PVC is considered as a vital polymer, the development of the PVC compounds is due to the consistent expansion of its application fields [21].

In this paper we report the synthesis and characterization of new 1,3,4-oxadiazole, 1,2,4-triazole derivatives and their PVC polymers in good yield and study of the biological activity for these compounds.

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2.EXPERIMENTAL SECTION:

2.1.Materials:

The organic compounds supplied in high purity**: All used chemicals** are in the highest available purity (99.98 %) . All the starting materials used in this paper were take up from Sigma- Aldrich Company.

2.2.Instrumentation:

The chemical identification performed on techniques like Melting points were determined on a Gallenkamp (MFB-600-) Melting point Stuart apparatus, FT-IR spectra were recorded on a Bruker spectrometer (400- 4000) in KBr -disc., ^{1}H.NMR– Spectra and ^{13}C.NMR - Spectra were recorded on a Bruker (AC 400)NMR spectrometer, operating at (400 MHz) for ^{1}H-NMR and (100 MHz) for **^{13}C-NMR**. All chemical shifts (δ) are reported in ppm relative to tetramethylsilane (TMS) as reference (δ=0.0 ppm).

2.3.Procedures:

2.3.1. *Synthesis of 4-((4-hydroxy-3-methylnaphthalen-1-yl)diazenyl)benzoic acid [M1] [22]:*

(0.01 mole, 1.37 g) P-amino benzoic acid dissolved in (10 ml) distill water and (5 ml) HCl, the temperature kept at (0 °C). Then, $NaNO_2$ dissolved in (10 ml) distill water and added dropwise to the mixture. The mixture was left for (15) min., this diazonium solution was added drop wise to coupling component solution which was prepared by mixing (0.01 mole, 1.57g) of 3-methyl-4-methyl naphthol in absolute ethanol and (1 g) of sodium hydroxide in (100 ml) distilled water, the precipitate then was filtered and washed with water many times. The product was purified by silica gel column chromatography eluting with DCM: Hexane (80:20, v/v) to afford brown solid of [M1].

2.3.2. *Synthesis of Ethyl 4-((4-hydroxy-3-methylnaphthalen-1-yl)diazenyl)benzoate [M2] [23]:*

To solution of (0.01 mole, 3.06 g) of compound [M1] in (100 ml) absolute ethanol, (15 ml) concentrated sulfuric acid was added as drop wise. The mixture was refluxed for (4) hours, the reaction content was poured into ice water, the precipitate was filtered and washed with water. The product was purified by silica gel column chromatography eluting with DCM: Hexane (80:20, v/v) to afford dark brown solid of [M2].

2.3.3. *Synthesis of 4-((4-hydroxy-3-methylnaphthalen-1-yl)diazenyl)benzoic acid hydrazide [M3] [24]:*

To solution of (0.01 mole, 3.06 g) of compound [M1] in (100 ml) absolute ethanol, (15 ml) concentrated sulfuric acid was added as drop wise. The mixture was refluxed for (4) hours, the reaction content was poured into ice water, the precipitate was filtered and washed with water. The product was purified by silica gel column chromatography eluting with DCM: Hexane (80:20, v/v) to afford dark brown solid of [M2].

2.3.4. *Synthesis of 5-((4-(4-hydroxy-3-methylnaphthalen-1-yldiazenyl))phenyl)-1,3,4-oxadiazole-2-thiol [M4] [25]:*

(0.01 mole, 3.2 g) compound [M3] was mixed with (0.01 mole, 0.56g) Potassium hydroxide (KOH) and excess of carbon disulfide (CS_2) in absolute ethanol was added. Then the mixture was refluxed for (8) hr. after that the solvent was evaporated, and then the distill water was added and the remain was dissolve in 30% HCl solution to preserve pH at 5-6. The precipitate then filtered and washed with water four times. The product was purified by silica gel column chromatography eluting with P.Ether:$CHCl_3$ (80:30, v/v) to afford black solid of [M4].

2.3.5 Synthesis of 5-((4-(4-hydroxy-3-methylnaphthalen-1-yldiazenyl))phenyl)-4H-1,2,4-triazole-3-thiol [M5] [26]:

A mixture of [M3] (0.01 mole, 3.20g), (0.01 mole, 0.91g) thiosemicarbazide, 10% NaOH solution (10 ml) refluxed for (12) hours. Then, the solution neutralized with 30% HCl, the precipitate was filtered and washed with water, then recrystallized by ethanol.

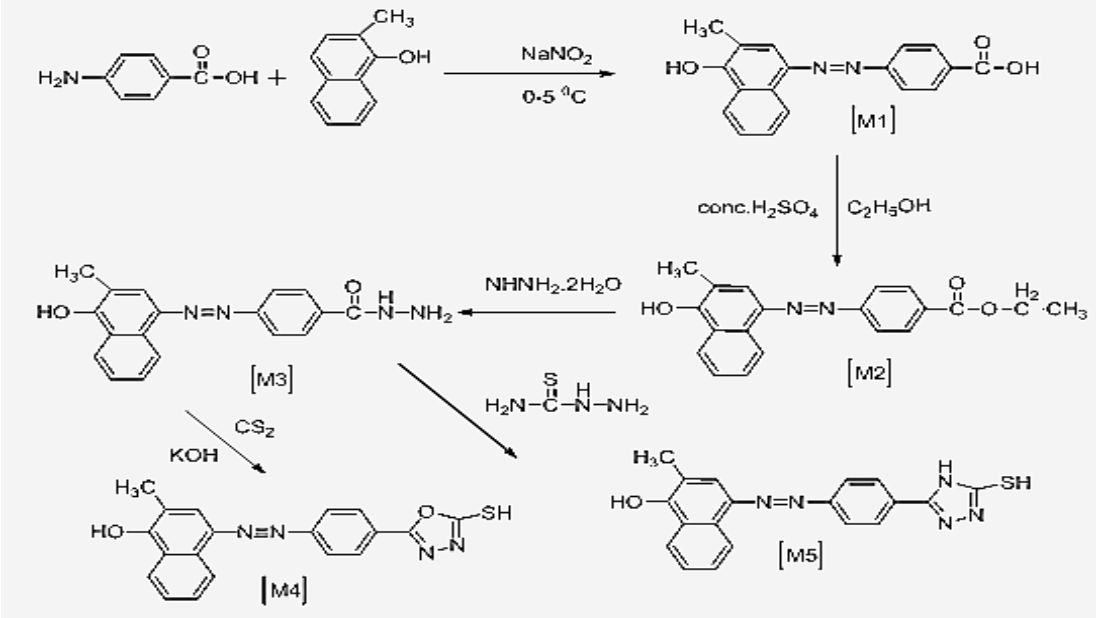
The product was purified by silica gel column chromatography eluting with Hexane: Ethyl acetate (1:1, v/v) to afford brown solid of [M5].

2.3.6 Synthesis of Compounds [M6 - M7] [27]:

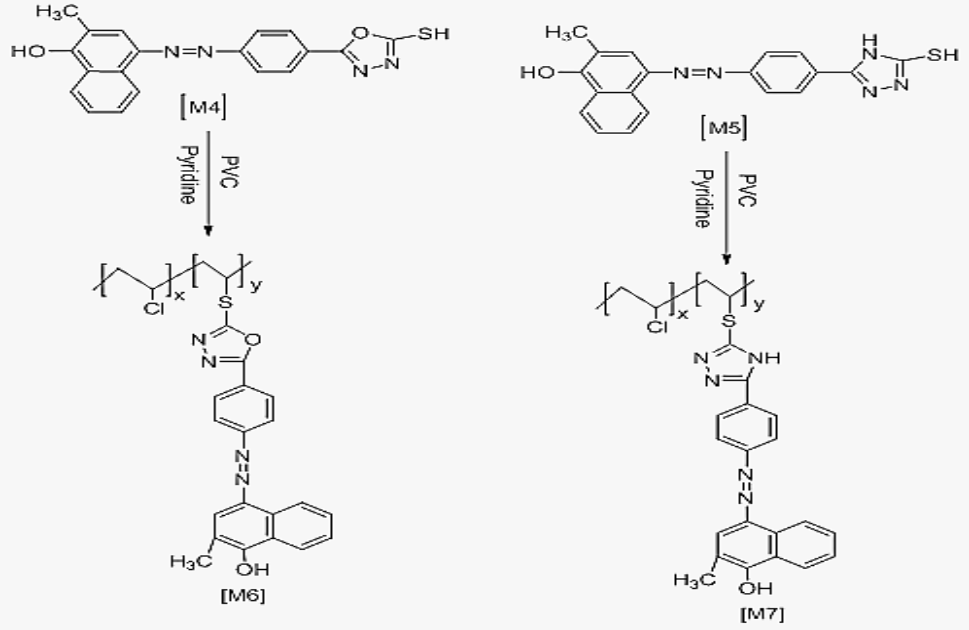
(0.15g) Poly (vinyl chloride) was dissolved in (16 mL) THF and (0.397g, 0.001 mole) compound [M4], and (0.40g, 0.001 mole) [M5] was added separately. (6) Drops of pyridine was added, then refluxed for (6) hours at (66) °C and filtered off, then the product was washed with water many time. Compound [M6], color: brown, m.p.=decompose >300 °C, Compound [M7], color: black, m.p.= decompose >300.

Maintenance of Cell Cultures

In RPMI-1640 supplemented with 10% Fetal bovine serum, 100 units/mL penicillin, and 100 µg/mL streptomycin, Michigan Cancer Foundation-7 cells were preserved. Cells were passage twice a week, with Trypsin-EDTA maintained at 80% confluence and incubated at 37 °C.



Scheme 1. Preparation route of compounds [M1-M5]



Scheme 2. Preparation route of compounds [M6, M7]

3.RESULTS AND DISCUSSION:

1,3,4-oxadiazole-5-thiol and 1,2,4-triazole derivatives were prepared from azo compound. Azo compound converted to ester compound that reacted with hydrazine. Carbon disulfide used in cyclization reaction to give compound [M4], also compound [M3] cyclized by sodium hydroxide to afforded compound [M5] (scheme 1).

The structure of these compounds has been characterize by FT-IR, ^{1}H-NMR and ^{13}C-NMR techniques, and elemental analysis. The data of these measurements were presented in tables 1,2 and3:

3.1.Spectral Investigation:

FT.IR-Spectra of Organic Compounds: The FTIR spectrum of compound [M1] exhibit a new absorption band at 1581 cm^{-1} corresponding to N=N and disappearance absorption band at 3458-3360 cm^{-1} for NH_2.

The FTIR spectrum for compound [M2] showed disappearance of C=O carboxylic acid at 1735 cm^{-1} and appearance C=O ester at 1704 cm^{-1}.

For compound [M3], the FTIR spectrum show absence absorption band at 1704 cm^{-1} for C=O ester

and appear new absorption band for C=O amid at 1680 cm^{-1}., 1,3,4- oxadiazole was synthesized from cyclization of hydrazide compound which exists in tautomeric thiol-thione equilibrium, as indicated by C=S stretching band at 1263 cm^{-1} and S-H stretch at 2450 cm^{-1}, and disappearance peak of C=O amide at 1680 cm^{-1}. Also, compound [M3] which upon ring closure with NaOH gave compound [M5].

compound [M5] exists in tautomeric thiol-thione equilibrium, which specific by C=S stretching band at 1230 cm^{-1} and S-H stretch at 2450 cm^{-1}. , Synthesis of new modified PVC containing 1,3,4-oxadiazole derivative and 1,2,4-triazole derivative with a view to appear the effect of introducing these moieties on chemical and physical properties of PVC (scheme 2).

This reaction was begin by attack the nucleophilic of (S, N) atoms on the carbon carrying chlorine atom in the polymeric chain, after that chloride anion departure as a good leaving group.

Compound [M6], FT.I.R spectrum shows disappearance absorption band at (2450) cm^{-1} of SH and appearance of absorption band of C-$H_{aliph.}$ at (2916, 2848) cm^{-1}.

While compound [M7], FT.I.R spectrum exhibited absorption band of N-H at (3255) cm^{-1} and disappearance absorption band at (2450) cm^{-1} of SH, that emphasized the reaction proceeded mainly by the attack of the S nucleophile and not the N and gave only one product. Also, appearance absorption band of C-$H_{aliph.}$ at (2916, 2848) cm^{-1} [23-27]. ,all bands abstracted in Table (1) .

Table 1: FT.IR- data (cm^{-1}) of Organic Compounds [M1-M7]

Comps	Other Groups
[M1]	(O-H): 3300 , (C-$H_{Ar..}$): 3045.45, (C=$O_{carboxylic\ acid}$): 1735.81, (N=N): 1581.52.
[M2]	(O-H): 3250, (C-$H_{Ar.}$): 3029.38, 2909.38, (C-$H_{alph.}$): 2906.45, (C=O_{ester}): 1704.96, (N=N): 1496.05, (C=$C_{Ar..}$): 1560.45
[M3]	(O-H): 3446.65, (NH, NH_2): 3299.60-3282.50,3164.26, (C=O_{amide}): 1680.60, (N=N): 1556.54.
[M4]	(O-H): 3240.19, (C-$H_{Ar..}$): 3087.82, (S-H): 2450, (C=N): 1685.74, (N=N): 1487.01.
[M5]	(O-H): 3250, (N-H): 3208.80, (C-H_{Ar}): 3091.60, (SH): 2450, (C=N.): 1664.66, (N=N): 1419.51.
[M6]	(C-$H_{Ar.}$): 3060, (C-$H_{alph.}$): 2916, 2848, (C=N): 1593, (C=$C_{Ar.}$): 1693, (N=N): 1542.
[M7]	(C-$H_{Ar.}$): 3066, (C-$H_{alph.}$): 2916, 2848, (C=N): 1599, (C=$C_{Ar.}$): 1696, (N=N): 1594.

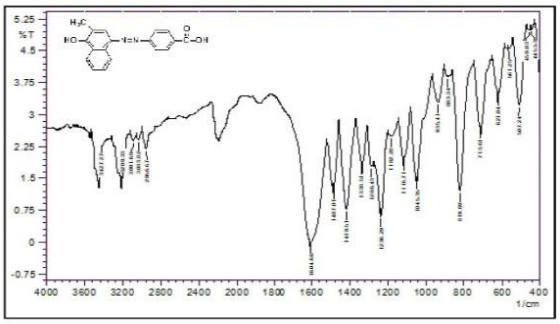


Figure 1: FTIR of compound [M1]

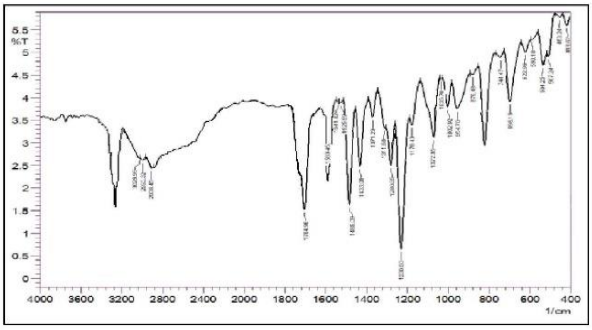


Figure 2: FTIR of compound [M2]

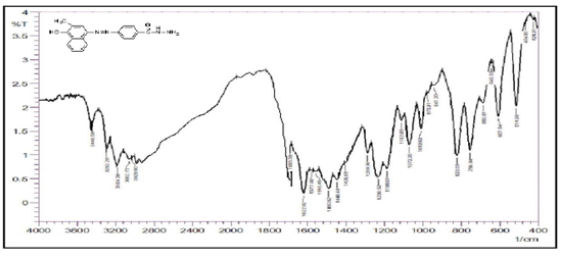


Figure 3: FTIR of compound [M3]

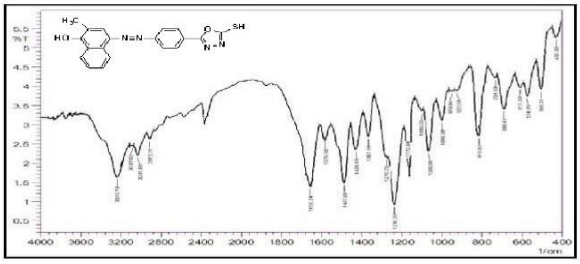


Figure 4: FTIR of compound [M4]

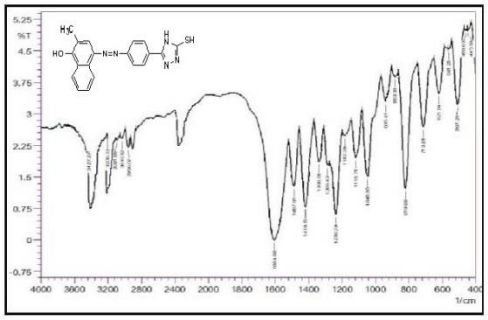


Figure 6: FTIR of compound [M6]

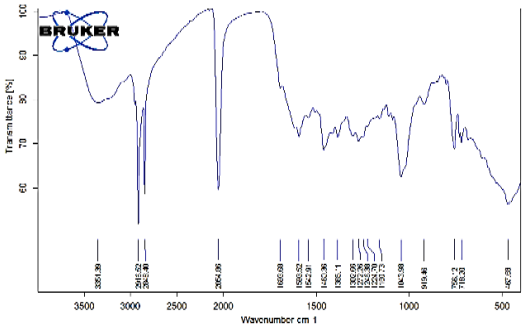


Figure 5: FTIR of compound [M5]

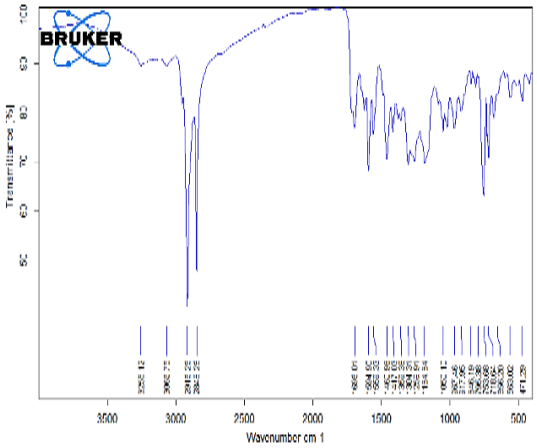


Figure 7: FTIR of compound [M7]

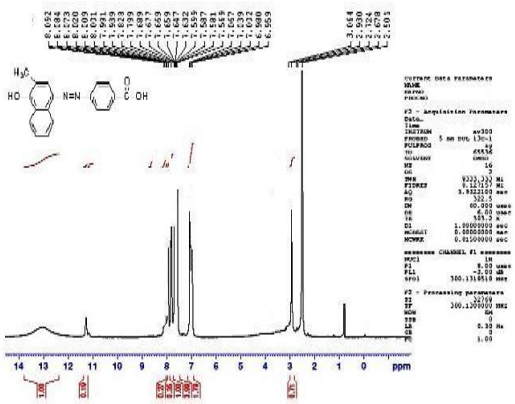


Figure 8: ^{1}H-NMR of compound [M1]

^{1}H.NMR- Spectra of Compounds : It gave many signals at б DMSO-d6(solvent): 2.50 .,(-CH_3) Protons at 9.0.,(COOH-) proton at 5.80., in compound [M1] .,while it showed signals at (-CH_2-) Protons at 1.83 and signals for (-CH_3) at 1.39 in compound [M2]. In hydrazide derivatives [M3] showed signals at 8.63 for proton of (NH_2).,(NH-) proton signal at 6.98. in oxadiazole compound , Protons of thiol appeared at 11.94. while in compound [N5], signal of proton of thiol (SH) appeared at 11.85, proton of (NH-) triazole at 5.6 . in compound [M6] , appearance signals for (CH_2-) of Poly vinylchloride at 1.19-4.45 and disappearance signal of hydrogen of thiol. appearance signals of (CH_2) of PVC at 1.17-4.73 and disappearance peak of hydrogen of thiol (SH) in compound [M7], Also the proton of Phenolic (-OH) appeared at (9.20 and 8.90) respectively in both compounds.

Table 2: H.NMR-data (б - ppm) of Compounds [M1-M7]

Comps	Other groups
[M1]	DMSO-d6(solvent): (3H, CH_3): 9.0, (H, Ar-H): 6.90-8.0, (H, Ar- OH): 8.09, (H, COOH): 11.20 .
[M2]	DMSO-d6(solvent): (3H, CH_3): 1.09, (3H, CH_3): 1.39, (2H_2, CH_2): 1.83, (H, Ar-H): 6.46-7.68, (H, Ar-OH): 11.10.
[M3]	DMSO-d6(solvent): (3H, CH_3): 1.98, (H, NH): 6.98, (H, ,Ar-H): 7.04- 8.08, (H, N-H_2): 8.63.
[M4]	DMSO-d6(solvent): (3H, CH_3): 1.55, (H, Ar-H): 6.63-7.65, (H, OH): 11.49, (H, SH)11.94.
[M5]	DMSO-d6(solvent): (3H, CH_3): 1.06, (H, NH): 5.60, (H, Ar-H): 6.46-7.64, (H, OH): 11.10, (H, SH): 11.85.
[M6]	DMSO-d6(solvent): (CH_3): 0.82, (H, CH, CH_2) for PVC :1.19-4.45, (H, Ar-H): 6.60-8.10, (H, OH): 9.20.
[M7]	DMSO-d6(solvent): (CH_3): 0.84, (H, CH, CH_2) for PVC :1.17-4.73, (H, OH): 8.90, (H, Ar-H)6.95-8.45.

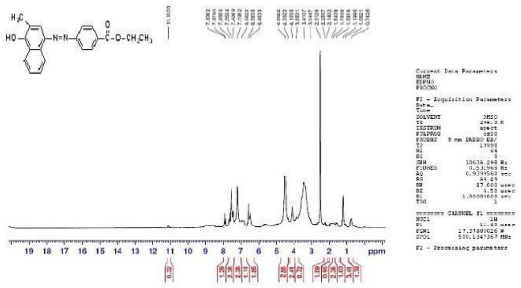


Figure 9: ^{1}H-NMR of compound [M2]

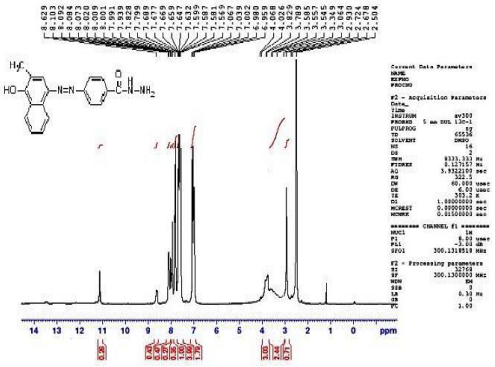


Figure 10: ^{1}H-NMR of compound [M3]

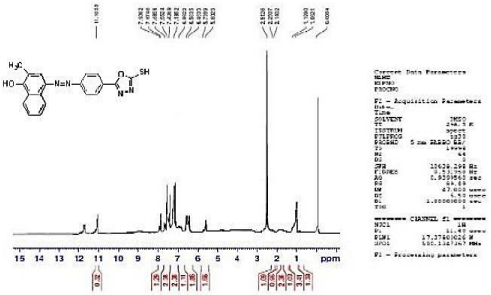


Figure 11: ^{1}H-NMR of compound [M4]

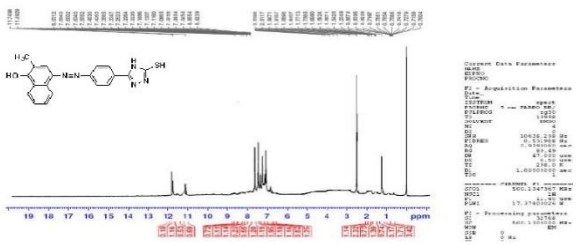


Figure 12: ^{1}H-NMR of compound [M5]

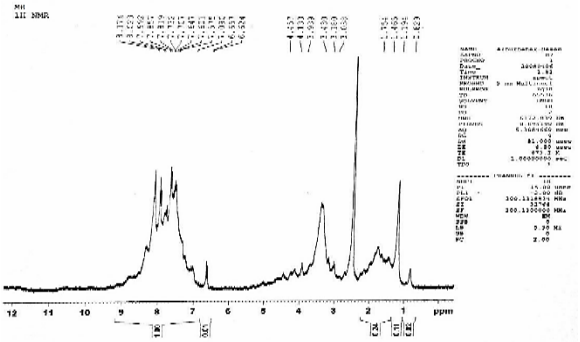


Figure 13: ^{1}H-NMR of compound [M6]

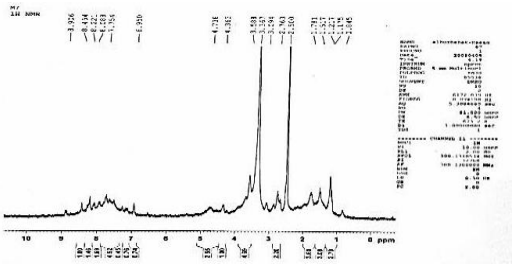


Figure 14: ^{1}H-NMR of compound [M7]

The ^{13}C.NMR spectral :All spectra appeared new signals indicate to formation of new organic compounds and new functional groups[8] in these compounds, table (3):

Compound [M1]:(40.0) for solvent (DMSO) ., 16.0 (C, CH_3), 116.0-130.0 (C, Ar-C), 182.0 (C, C=O).

Compound [M2]: (40.0) for solvent (DMSO) ., 8.0 (C, CH_3), 21.0, (C, CH_3), 22.0(C, CH_2), 110.0-131.0 (C, Ar-C), 170.0 (C, C=O).

Compound [M3]: (40.0) for solvent (DMSO) ., 10.0 (C, CH_3), 111.0 -132.0 (C, Ar-C), 180.0 (C, C=O).

Compound [M4]: (40.0) for solvent (DMSO) ., 24.0 (C, CH_3), 112.0-136.0 (C, Ar-C), 144.0-146.0 (2C, 2CH).

Compound [M5]: 28.0 (C, CH_3), 108.0-132.0(C, Ar-C), 146.0-148.0 (2C, 2CH).

Table 3: ^{13}C.NMR- data of Compounds

Comps.	^{13}C.NMR-data ((Only Important Peaks))
[M1]	(C, CH_3): 16.0 , (C, Ar-C) :116.0-130.0, (C, C=O) :182.0.
[M2]	(C, CH_3) :8.0, , (C, CH_3): 21.0, (C, CH_2): 22.0, (C, Ar-C): 110.0-131.0, (C, C=O): 170.0.
[M3]	(C, CH_3): 10.0, (C, Ar-C): 111.0 -132.0, (C, C=O): 180.0 .
[M4]	(C, CH_3): 24.0, (C, Ar-C): 112.0-136.0, (2C, 2CH): 144.0-146.0.
[M5]	(C, CH_3): 28.0, (C, Ar-C): 108.0-132.0, (2C, 2CH):146.0-148.0

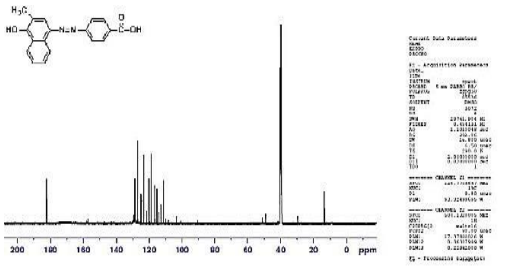


Figure 15: ^{13}C-NMR of compound [M1]

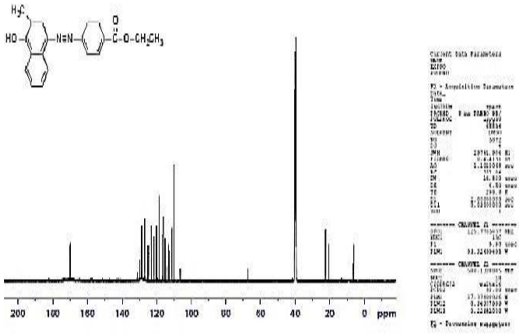


Figure 16: ^{13}C-NMR of compound [M2]

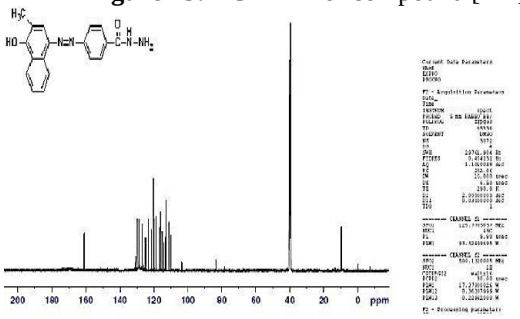


Figure 17: ^{13}C-NMR of compound [M3]

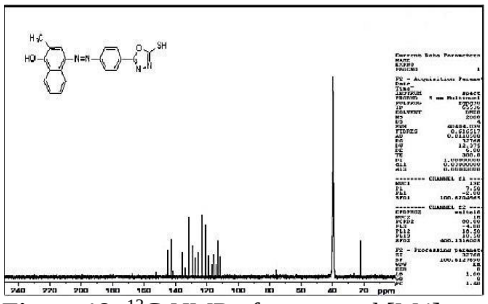


Figure 18: ^{13}C-NMR of compound [M4]

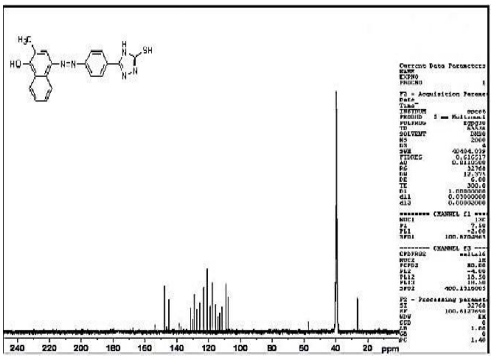


Figure 19: ^{13}C-NMR of compound [M5]

4. BIOLOGICAL ACTIVITY:

4.1 Cytotoxicity Assays

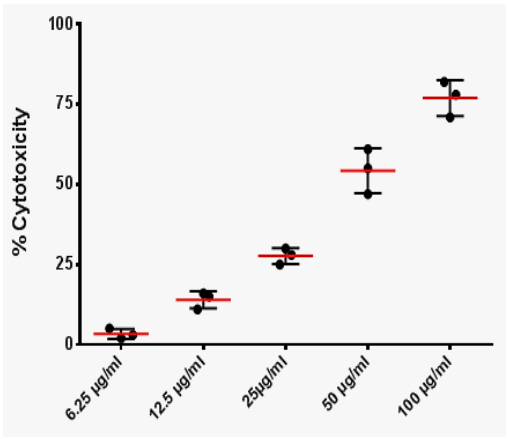
The MTT cell viability assay was made using 96-well plates to assess the cytotoxic effect of (M6, M7). At 1 × 10^4 cells/well, cell lines were seeded.24 hours later. Cells were treated with tested compounds at various constration, or a confluent monolayer was reached. After 72 hours of treatment, cell viability was determined by removing the medium, adding 28 µL of 2 mg/ ml of MTT solution incubating the cells at 37 ^{0}C for 2.5h. Following the removal of the MTT solution, the remaing crystals in the wells were solubilized by adding 130 µL of DMSO (DiMethyl Sulphoxide) accompanied by incubation at 37 37 ^{0}C for 15 minute with shaking [28-30].

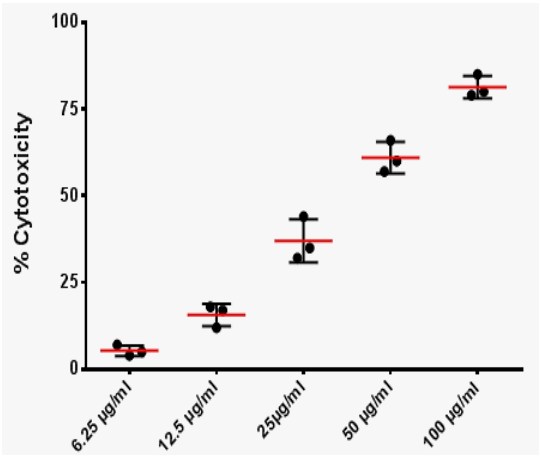
On a microplate reader at 492 nm, the absorbency was determined, the assay was carried out in triplicate. The inhibition rate of cell growth was determined as the following equation (the percentage of cytotoxicity) [31-36]:-

Cytotoxicity = A-B/A *100

where the optical control density and optical test density are A and B, with an unpaired t-test with GraphPad Prism 6, the data obtained was statically analyzed. The values of the triplicate measurments were described as mean ± SEM [30]**.**

MCF-7 is a breast cancer cell line evaluated the anti-proliferating effect of drug-loading M6 and M7 against the breast cancer cell lines. Based on cytotoxicity analyses, it concluded that prepared compounds M6 and M7 may be an appropriate and promising strategy for developing effective drug delivery system to clinical application against breast cancers. in M6 (IC_{50}=25.76 µM/ml) and M7 (IC_{50}=21.41 µM/ml), the IC_{50} value was substantially decreased compared with pure drugs and the induced apoptotic cell death pathway. The finding of this study indicate that the M6 and M7 could be used for medical applications and include a beneficial chemotherapy formulation (figures 1 and 2).





Cytotoxic effect of M6 (**Figure 20,** IC_{50}=25.76 µM/ml) and M7 (**Figure 21,** IC_{50}=21.41 µM/ml) in MCF-7 cells.

4.2 The antibacterial activity

The antibacterial activity of synthesized compounds [M4-M7] was summarized in table 4 (figures 22 and 23). This activity was tested by the agar disc-diffusion method against gram positive Bacterial (*Streptococcus and Staphylococcus*), gram negative Bacterial (*Moraxella and E. Coli*) . Dimethyl sulphoxide (DMSO) was used as solvent control, and the concentration of the tested compounds was 10^{-3} M. The results of these study shows that (M4 and M7) have a good anti-Bacterial activity [31,36-37] due to their structure that form interaction with wall of cell in selected bacteria which caused high inhibition.

Table 4. Antibacterial activity of compounds M4-M7

Compound number	Streptococcus	Staphylococcus	Moraxella	E. Coli
[M4]	15	26	25	14
[M5]	0.0	15	0.0	0.0
[M6]	22	20	10	9
[M7]	33	35	18	20

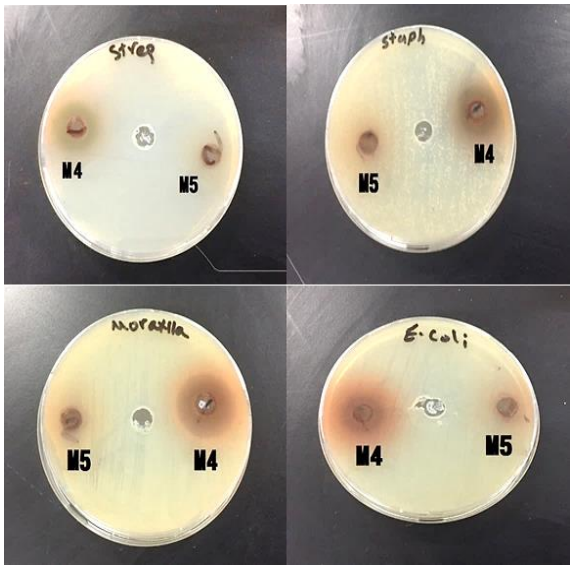


Figure.22: Effect of compounds M6 and M7 on Streptococcus, Staphylococcus, *Moraxella and E. Coli*

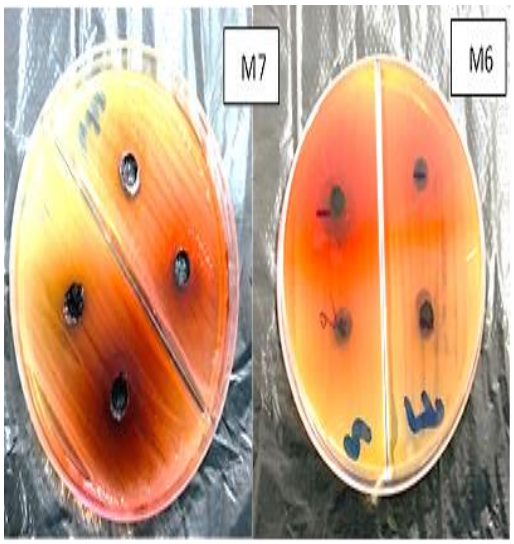


Figure23: Effect of compounds M4 and M5 on *Streptococcus, Staphylococcus, Moraxella and E. Col*

5.Physical and Chemical Properties of Formatted Compound [M1-M7]:

The formatted organic compounds appeared some physical properties which summarized in table (5):

Table 5: Physical properties for prepared compounds [M1-M5]

Comp. No.	M.F	M.Wt g mole^{-1}	colour	M.P.	yield	TLC solvent	R_f
[M1]	$C_{18}H_{14}N_2O_3$	306	Brown	290-292	92%	Hexane:DCM 3:2	0.66
[M2]	$C_{20}H_{18}N_2O_3$	334	Dark brown	133-135	89%	Hexane:DCM 3:3	0.64
[M3]	$C_{18}H_{16}N_4O_2$	320	Brown	143-145	88%	Perrolum ether:$CHCl_3$ 4:2	0.54
[M4]	$C_{13}H_{15}N_5OS$	361	Black	267-269	80%	Perrolum ether:$CHCl_3$ 4:2	0.62
[M5]	$C_{14}H_{17}N_5OS$	362	Brown	316-318	83%	Hexane:ethylacetate 3:3	0.78
[M6]	-	-	Brown	>300			
[M7]	-	-	black	>200			

Table 6:. C.H.N.S data of the prepared compounds [M1-M5]

COMP NO.	C%		H%		N%		S%	
	Calcul.	Measur	Calcul.	Measur.	Calcul.	Measur.	Calcul.	Measur.
[M1]	70.588	70.60	4.575	4.588	32.026	32.034	-	-
[M2]	71.856	71.87	5.389	5.40	8.383	8.41	-	-
[M3]	67.5	67.62	5.0	5.10	17.50	17.53	-	-
[M4]	64.640	64.671	3.867	3.885	13.259	13.281	8.839	8.855
[M5]	63.157	63.16	4.155	4.160	19.395	19.420	8.864	8.871

6.Conclusions : 1,3,4-Oxadiazole-5-thiol [M4] and 1,2,4-Triazole [M5]compounds were synthesized from azo compound. New modified PVC containing 1,3,4-oxadiazole and 1,2,4-triazole derivatives were synthesized. The biological activity for target molecule were evaluated as antibacterial candidates and against breast cancer cell lines based on cytotoxicity analyses. Hybrid polymers [M6] and [M7] may be an appropriate and promising strategy for developing effective drug delivery system to clinical application against breast cancers.

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الخلاصة:

في هذا العمل ، تم تحضير مشتقات Triazole-1،2،4 و Oxadiazole-1،3،4 من [4- (4-4-hydroxy-3-methyl naphthyl) diazenyl] حامض البنزويك [M1] ، والذي تم تحويله إلى [4- (4-هيدروكسي 3-ميثيل نافثيل) ديازينيل] بنزوات [M2]. يتفاعل مشتق البنزوات مع الهيدرازين الممنوح [M3] والذي يتحولق بواسطة ثاني كبريتيد الكربون لإعطاء المركب [M4]. بالإضافة إلى ذلك ، تحولق المركب [M3] الذي تم تحقيقه بواسطة هيدروكسيد الصوديوم وثيوسيميكاربازيد لإعطاء تريازول - ثيول [M5]. تم تحضير البوليمرات المتجانسة [M6 و M7] عن طريق تفاعل[M4] (oxadiazole -1،3،4) و [M5] (triazole- 4،2،1) بشكل منفصل مع بولي فينيل كلورايد في وجود البيريدين ورباعي هيدروفيوران. شخصت هذه المركبات بالتقنيات التالية: FT-IR و ^{1}H و$CNMR^{13}$ و elemental analysis C,H,N,S. الفعالية البيولوجية، تم تخفيض قيمة IC_{50} بشكل ملحوظ في M6 (IC_{50} = 25.76 ميكرومتر / مل) و M7 (IC_{50} = 21.41 ميكرومتر / مل). أيضا، تم دراسة النشاط البيولوجي ضد البكتريا للنواتج النهائية واعطت نتائج جيدة نتائج جيدة.