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SYNTHESIS AND ANTIMICROBIAL ACTIVITY OF SOME NEW QUINOLINE DERIVATIVES

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ABSTRACT

Two series of novel quinoline derivatives; oxadiazolyl and thiadiazolyl quinolines were prepared and evaluated for their antimicrobial activities. The first series; 5-(2-aryl-6-substituted-4-quinolyl)-1,3,4-oxadiazol-2-amines (V_{a-g}) was synthesized by cyclization of the key intermediate thiosemicarbazides (IV_{1-7}). The second one; 5-(2-aryl-6-substituted-4-quinolyl)-1,3,4-thiadiazol-2-amines ($VI_{a,c,f,g}$) was synthesized through cyclization of the key intermediate quinoline-4-carboxylic acids (I_{1-7}) or from the synthetically accessible thiosemicarbazides (IV_{1-7}).The target oxadiazole and thiadiazole derivatives were evaluated against Gram positive, Gram negative bacteria and fungi. The obtained results showed that the 1,3,4-thiadiazoles $VI_{4,8}$ exhibited the most potent antibacterial activity with MIC values of 4 μg/ml.

INTRODUCTION

Quinoline derivatives display diverse biological activities including antimicrobial[1,2], antifungal[3], antiamoebic[4], antimalarial[5] and hepatitis C virus inhibitors[6]. On the other hand, 1,3,4-oxadiazole derivatives have shown antimicrobial[7-10], anti-inflammatory[11] and antifungal activities[12,13]. In addition, 1,3,4-thiadiazoles were extensively reported to have appreciably potent antimicrobial activities[14,15].

In this work, new quinoline derivatives containing 1,3,4-oxadiazoles and 1,3,4-thiadiazoles were prepared with the aim to possess superior antimicrobial activities.

EXPERIMENTAL

Melting points were determined with Gallenkamp Digital melting point apparatus in open capillaries and are uncorrected. IR spectra (kBr) were recorded using a Pye Unicam SP1000 IR Spectrometer (ν, cm^{-1}).

^{1}H-NMR spectra were determined on a varian-Mercury 200 MHz spectrometer using $CDCl_3$ or DMSO-d_6 as solvents and TMS as internal standard (chemical shift in δ, ppm). Mass spectra were measured on an HP 5995 instrument Faculty of Science Cairo University, Egypt. Elemental analyses were performed at the National Research Center, Cairo, Egypt. TLC was performed on silica gel G (Merk) and spots were visualized by irradiation with UV light (254 nm). Compounds I_{a-j}, $II_{a,b,d,e,g,i,j}$, $III_{a,b,d,e,g,i,j}$ were prepared according to reported procedures[16,17].

2[(2-Aryl-6-substituted-4-quinolyl)carbonyl]-1-hydrazine carbothiamides ($IV_{a,b,d,e,g,i,j}$)

A suspension of the appropriate 2-arylquinoline-4-carbohydrazides (III_{1-7}) (10 mmol), potassium thiocyanate (1.984, 20 mmol), and hydrochloric acid (36%, 10ml) in water (200 ml) was heated at reflux for 3.5 h. After cooling, the white solid was filtered, washed with water, and dried. The crude product was purified by recrystallization from aqueous ethanol (1).

^{1}H-NMR of compound IV_a (DMSO-d_6) δ: 7,50-7.60 (m, 4H, Ar-H), 7.80-8.00 (m, 2H, Ar-H), 8.20-8.40 (m, 5H, NH_2, Ar-H), 8.70-8.80 (d, 1H, Ar-H), 9.47 (s, 1H, NH), 9.80 (s, 1H, NH). IR of compound IV_2 (kBr,cm^{-1}): 3431, 3308, 3266, 3197 (2NH + NH_2), 1671 (C=O), Compound IV_b ^{1}H-NMR (DMSO-d_6) δ: 5.67 (s, br, 4H, NH_2+2NH), 7.10-7.20 (d, 2H, ArH), 7.80-7.90 (dd, 2H, Ar-H), 8.10-8.30 (m, 3H, Ar-H), 8.55 (s, 1H, Ar-H), 9.18 (s, 1H, Ar-H).

^{1}H-NMR of compound IV_d (DMSO-d_6) δ: 2.44 (s, 3H, CH_3), 7.60-7.70 (m, 4H, Ar-H), 7.80-8.00 (m, 4H, Ar-H, NH_2-exchangeable), 8.55 (s, 1H, Ar-H), 9.55 (s, 1H, NH, exchangeable), 10.72 (s, 1H, NH, exchangeable).

^{1}H-NMR of compound IV_e (DMSO-d_6) δ: 3.98 (s, 3H, OCH_3), 7.10-7.30 (m, 4H, Ar-H, NH_2), 7.60-7.70 (m, 1H, Ar-H), 7.80-7.90 (m, 2H, Ar-H, NH), 8.10-8.20 (m, 2H, Ar-H, NH), 8.30-8.40 (d,2H, Ar-H), 8.50-8.60 (d, 2H, Ar-H).

IR of compound IV_g (kBr, cm^{-1}): 3428, 3311, 3229, 3197 (NH_2+2NH), 1671 (C=O).

^{1}H-NMR of compound IV_g (DMSO-d_6) δ: 5.18 (s, 4H, NH_2 + 2NH, exchangeable), 7.50-7.67 (d, 1H, Ar-H), 7.72-7.80 (m, 2H, Ar-H), 7.85-7.95 (m, 1H, Ar-H), 8.20-8.30 (m, 3H, Ar-H), 9.10-9.20 (d, 1H, Ar-H).

^{1}H-NMR of compound IV_i (DMSO-d_6) δ: 2.41 (s, 3H, CH_3), 4.71 (s, 4H, NH_2+2NH), 7.30-7.50 (m, 3H, Ar-H), 7.70-7.80 (d, 1H, Ar-H), 7.90-8.00 (d, 1H, Ar-H), 8.10-8.18 (m, 1H, Ar-H), 8.22-8.30 (d, 1H, Ar-H), 8.36 (s, 1H, Ar-H).

^{1}H-NMR of compound IV_j (DMSO-d_6) δ: 3.84 (s, 3H, OCH_3), 7.1-7.2 (d, 2H, Ar-H), 7.69-7.73 (m, 1H, Ar-H), 7.80-7.90 (m, 3H, Ar-H, NH_2), 810-826 (m, 3H, Ar-H, NH), 8.48-8.52 (d, 1H, Ar-H), 11.12 (s, 1H, NH).

5-(2-Aryl-6-substituted-4-quinolyl)1,3,4-oxadiazol-2-amines (V_{1-7})

To a suspension of the appropriate 2[(2-aryl-6-substituted-4-quinolyl)carbonyl]-1-hydrazine carbothiamides IV_{a-g} (1.5 mmol), in ethanol (95%, 50 ml), sodium hydroxide (4N, 7.55 ml) was added and the mixture was allowed to stir till give a clear solution. Iodine in potassium iodide solution (5%) was then added until the color of iodine persisted

and the mixture was heated at reflux for 3h. The reaction mixture was poured into ice-water, and the resulting precipitate was filtered, washed with water and warm carbon disulphide. The crude product was recystallized from absolute ethanol (Table 2).

^{1}H-NMR of compound V_a (DMSO-d_6) δ: 7.40-7.60 (m, 3H, NH_2, Ar-H), 7.68-7.79 (m, 2H, Ar-H), 7.82-7.90 (m, 2H, Ar-H), 8.00-8.18 (d, 1H, Ar-H), 8.20-8.30 (d, 1H, Ar-H), 8.35-8.40 (d, 1H, Ar-H), 8.45 (s, 1H, Ar-H), 9.10-9.20 (d, 1H, Ar-H).
IR of compound V_b (kBr, cm^{-1}): 3113 (NH_2).

^{1}H-NMR of compound V_b (DMSO-d_6) δ: 7.40-7.55 (m, 3H, Ar-H, NH_2, exchangeable), 7.65-7.78 (m 2H, Ar-H), 7.80-7.90 (m, 2H, Ar-H), 8.10-8.30 (m, 3H, Ar-H), 9.10-9.20 (d, 1H, Ar-H)
MS of compound V_b (m/z): 368, 367, 366 (M^{+2}, M^{+1}, M^+, 91.8, 16.8, base peak), 325 (21.7%), 284 (30.3%), 243 (21.1%), 203 (56.6%), 101 (43.6%), 75 (37.0%).
IR of compound V_d (kBr, cm^{-1}): 3284, 3078 (NH_2).

^{1}H-NMR of compound V_g (DMSO-d_6) δ: 7.40-7.50 (d, 1H, Ar-H), 7.55-7.70 (m, 3H, NH_2, Ar-H), 7.80-7.90 (m, 1H, Ar-H), 8.10-8.20 (d, 2H, Ar-H), 8.80-8.90 (d, 1H, Ar-H).

Table (1): Physical and analytical data of 2[(2-aryl-6-substituted-4-quinolyl) carbonyl]-1 hydrazinecarbothiamides (IV_{a-g}).

Cpd	X	R	MP(°C)	Yield (%)	Mol. Formula (M.wt)	Analysis	
						Calcd%	Found%
IV_a	H	H	[211-213]	60	$C_{17}H_{14}N_4OS$ (322.385)	C=63.33, H=4.38 N=17.38	C=63.59, H=4.78 N=17.50
IV_b	H	Br	[229-230]	66	$C_{17}H_{13}BrN_4OS$ (401.28)	C=50.88, H=3.27 N=13.96	C=50.77, H=3.59 N=14.05
IV_c	H	CH_3	[217-218]	70	$C_{18}H_{16}N_4OS$ (336.41)	C=64.26, H=4.79 N=16.65	C=64.60, H=4.95 N=16.65
IV_d	H	OCH_3	[>300]	61	$C_{18}H_{16}N_4O_2S$ (352.41)	C=61.35, H=4.58 N=15.90	C=60.95, H=4.72 N=16.30
IV_e	Cl	Br	[264-265]	63	$C_{17}H_{12}BrClN_4OS$ (435.726)	C=46.86, H=2.78 N=12.86	C=47.28, H=2.70 N=12.40
IV_f	Cl	CH_3	[221-222]	72	$C_{18}H_{15}ClN_4OS$ (370.857)	C=58.3, H=4.08 N=15.11	C=58.25, H=4.50 N=15.13
IV_g	Cl	OCH_3	[295-296]	64	$C_{18}H_{15}ClN_4O_2S$ (386.856)	C=55.88, H=3.91 N=14.48	C=55.48, H=3.51 N=14.45

IR of compound IV_b (KBr, cm^{-1}): 3431, 3308, 3266, 3197 (2NH+NH_2), 1671 (C=O).
IR of compound IV_d (KBr, cm^{-1}): 3428, 3311, 3229, 3197 (2NH+NH_2), 1671 (C=O).

Table (2): Physical and analytical data of 5-(2-aryl-4-substituted)-1,3,4-oxadiazol-2-amines (V_{a-g}).

Cpd	X	R	MP(°C)	Yield (%)	Mol. Formula (M.wt)	Analysis	
						Calcd%	Found%
V_a	H	H	271-273	73	$C_{17}H_{12}N_4O$ (288.3)	C=70.82, H=4.20 N=19.43	C=70.56, H=3.82 N=19.11
V_b	H	Br	261-263	65	$C_{17}H_{11}BrN_4O$ (367)	C=55.61, H=3.02 N=15.26	C=55.40, H=3.06 N=14.89
V_c	H	CH_3	235-237	69	$C_{18}H_{16}N_4O$ (302.33)	C=71.51, H=4.67 N=18.53	C=71.61, H=4.29 N=18.89
V_d	H	OCH_3	256-258	66	$C_{18}H_{16}N_4O_2$ (318.33)	C=67.91, H=4.43 N=17.60	C=67.61, H=4.50 N=17.90
V_e	Cl	Br	280-282	70	$C_{17}H_{10}BrClN_4O$ (401.64)	C=50.84, H=2.51 N=13.95	C=51.30, H=2.73 N=14.00
V_f	Cl	CH_3	239-241	68	$C_{18}H_{13}ClN_4O$ (336.78)	C=64.19, H=3.89 N=16.64	C=63.97, H=4.07 N=16.60
V_g	Cl	OCH_3	252-255	71	$C_{18}H_{13}ClN_4O_2$ (352.77)	C=61.27, H=3.71 N=15.88	C=61.03, H=3.98 N=15.76

IR of compound V_a(KBr, cm^{-1}): 3113, 3063 (NH_2).
IR of compound V_c (KBr, cm^{-1}): 3284, 3078 (NH_2).

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5-(2-Aryl-6-substituted-4-quinolyl)-1,3,4-thiadiazol-2-amines(VI_{a-j}). These compounds were prepared by two methods:

Method A

To an ice cooled mixture of the appropriate 2-aryl-6-substituited quinoline-4-carboxylic acids ($I_{b-d,f,h-j}$) (50 mmol) and thiosemicarbazide (22.8 g, 2.5 m.mol), phosphorus oxychloride (3 ml) was slowly added and the mixture was warmed at 70° for 1 h. The reaction mixture was poured into ice water. The resulting precipitate was filtered, resuspended in water, neutralized with sodium hydroxide. The obtained solid was filtered, washed with water and dried. The crude product was purified by recrystallization from methanol to give VI_{a-j}.

Method B

A mixture of the appropriate of 2-[2-aryl-6-substituted-4-quinolyl) carbonyl]-1-hydrazine-carbothiamides ($IV_{b,c,f,g}$) and concentrated sulfuric acid (15 ml) was allowed to stir at room temperature for 16 h. The reaction mixture was poured into ice water, neutralized with liquid ammonia and the resulting precipitate was filtered. The product obtained was recrystallized from methanol to afford $VI_{b,d,j,j}$(Table 3).

^{1}H-NMR of compound VI_a (DMSO-d_6) δ: 7.60-7.75 (m, 3H, NH_2, Ar-H), 7.82-7.92 (m, 3H, Ar-H), 8.10-8.30 (m, 4H, Ar-H), 8.80-8.90 (d, 1H, Ar-H).
IR of compound VI_a (kBr, cm^{-1}): 3313, 3267 (NH_2).
^{1}H-NMR of compound VI_2 (DMSO-d_6) δ: 7.50-7.60 (d, 1H, Ar-H), 7.65-7.75 (m, 3H, NH_2, Ar-H), 7.80-7.90 (m, 2H, Ar-H), 8.10-8.20 (d, 2H, Ar-H), 8.26-8.35 (d, 2H, Ar-H), 8.80-8.90 (d, 1H, Ar-H).

^{1}H-NMR of compound VI_c ($CDCl_3$) δ: 2.6 (s, 3H, CH_3), 5.38 (br.s, 2H, NH_2), 7.50-7.67 (m, 2H, Ar-H), 7.70-7.90 (m, 2H, Ar-H), 8.0 (s, 1H, Ar-H), 8.10-8.20 (d, 2H, Ar-H), 8.25-8.35 (d, 1H, Ar-H), 8.80 (d, 1H, Ar-H).
IR of compound VI_c (kBr, cm^{-1}): 3284, 3078 (NH_2)

^{1}H-NMR of compound VI_d (DMSO-d_6) δ: 7.60-7.67 (d, 1H, Ar-H), 7.70-7.78 (m, 3H, NH_2, Ar-H), 7.80-7.90 (m, 2H, Ar-H), 8.10-8.20 (d, 2H, Ar-H), 8.30-8.40 (d, 2H, Ar-H), 8.80-8.90 (d, 1H, Ar-H).

^{1}H-NMR of compound VI_e (DMSO-d_6) δ: 4.8 (br.s, 2H, NH_2, exchangeable), 7.60-7.70 (m, 1H, Ar-H), 7.78-7.89 (m, 1H, Ar-H), 7.90-8.00 (d, 1H, Ar-H), 8.10-8.20 (d, 2H, Ar-H), 8.30-8.40 (d, 2H, Ar-H), 8.80-8.90 (d, 1H, Ar-H).

^{1}H-NMR of compound VI_f (DMSO-d_6) δ: 2.38 (s, 3H, CH_3), 7.30-7.40 (d, 2H, Ar-H), 7.60-7.80 (m, 3H, NH_2, Ar-H), 8.0 (s, 1H, Ar-H), 8.10-8.20 (d, 2H, Ar-H), 8.27-8.38 (d, 1H, Ar-H), 8.8 (d, 1H, Ar-H).

^{1}H-NMR of compound VI_g ($CDCl_3$) δ: 3.59 (s, 3H, OCH_3), 5.42 (br.s, 2H, NH_2), 7.50-7.56 (d, 1H, Ar-H), 7.60-7.69 (m, 1H, Ar-H), 7.72-7.93 (m, 1H, Ar-H), 8.0 (s, 1H, Ar-H), 8.13-8.16 (m, 2H, Ar-H), 8.26-8.37 (d, 1H, Ar-H), 8.70-8.80 (d, 1H, Ar-H).

MS of compound VI_a (m/z): 384 (M^{+2}, M^+, 2.9%, 25.3%), (100%), 261 (22.9%), 229 (25%), 203 (17.4%), 131 (12.1%), 101 (11.8%), 74 (45.4%).

Table (3): Physical and analytical data of 5-(2-aryl-4-quinolyl)-1,3,4-thiaziazol-2-amines (IV_{b-g}):

Cpd	X	R	MP(°C)	Yield (%)		Mol. Formula (M.wt)	Analysis	
				Method A	Method B		Calcd%	Found%
VI_a	H	Br	266-268	75	65	$C_{17}H_{11}BrN_4S$ (383.26)	C=53.37,H=2.89 N=14.62	C=53.19,H=2.70 N=14.71
VI_b	H	Cl	259-261	73	-	$C_{17}H_{11}ClN_4s$ (338.82)	C=60.26,H=3.27 N=16.54	C=61.50H=3.27 N=16.2
VI_c	H	CH_3	232-234	65	80	$C_{18}H_{14}N_4S$ (318.39)	C=67.9,H=4.43 N=17.6	C=67.25,H=4.30 N=11.30
VI_d	Cl	H	255-257	70	-	$C_{17}H_{11}ClN_4S$ (338.82)	C=60.26,H=3.27 N=16.54	C=54.85,H=3.39 N=16.56
VI_e	Cl	Cl	292-294	64	-	$C_{17}H_{10}Cl_2N_4S$ (373.26)	C=54.70,H=2.70 N=15.01	C=54.15,H=3.14 N=14.75
VI_f	Cl	CH_3	264-266	69	65	$C_{18}H_{13}ClN_4S$ (352.84)	C=61.27,H=3.71 N=15.88	C=61.29,H=3.52 N=15.13
VI_g	cL	OCH_3	244-246	68	60	$C_{18}H_{13}ClN_4OS$ (368.84)	C=58.61,H=3.55 N=15.19	C=58.36,H=3.39 N=15.00

IR of compound VI_a (KBr, cm^{-1}): 3313, 3267 (NH_2).
IR of compound VI_c (KBr, cm^{-1}): 3284, 3078 (NH_2).

2. Biology

Antimicrobial activity

2. Biology

Antimicrobial activity

The target oxadiazoles and thiadiazoles were evaluated against Staphylococcus aureus ATCC 25923, Bacillus subtilis ATCC 6633 as examples for Gram positive bacteria, Escherichia coli ATCC 10536, Salmonella typhimurium NCTC 14024 as examples for Gram negative bacteria, and Candida albicans ATCC 10231, Saccharomyces cerevisiae ATCC as representative of fungi.

The strains used in this study were maintained at the Microbiology Department, Faculty of Pharmacy, Zagazig University. After antimicrobial screening, the MIC was determined by using two-fold serial dilution method[14-16]. Ampicillin and Nystatin were used as reference standards to compare the antibacterial and antifungal activity, respectively. For determining both antibacterial and antifungal activity, the synthesized compounds and the control drugs were dissolved in a mixture of sterile water and dimethylformamide (8:2, the stock solution 5 mg/mL). Further dilutions were prepared at the required quantities of 400, 200, 100, 50, 25, 12.5, 6.25 and 3.125 µg/ml, concentrations. In order to ensure that the solvent had no effect on bacterial growth, a control test was also performed containing broth supplemented with only DMF at the same dilution used in our experiment. The MIC values were obtained from the lowest concentration of the test compound where the tubes remain clear, indicating that the bacterial growth was completely inhibited at this concentration. The MIC values were expressed in µg/ml and the results are shown in Table (4).

1. Antibacterial assay

The cultures were obtained in Mueller-Hinton broth for all the bacteria after 24 h of incubation at 37°C. Testing was carried out on Mueller-Hinton broth at pH 7.4 and the two-fold serial dilution technique was applied. The final inoculum size was 10^6 (colony forming units) CFU/mL. A set of tubes containing only inoculated broth was kept as control. After incubation for 24 h at 37°C, the last tube with no growth of microorganism was recorded to represent MIC expressed in µg/mL. Every experiment in the antibacterial assay was replicated twice in order to define the MIC values.

2. Antifungal assay

The yeasts were maintained in Sabouraud dextrose broth after incubation for 24 h at 35°C. Testing was performed in Sabouraud dextrose broth at pH 7.4 and the two-fold serial dilution technique was applied. The final inoculum size was 10^5 CFU/mL. A set of tubes containing only inoculated broth was kept as control. After incubation for 48 h at 35°C, the last tube with no growth of yeast was recorded to represent MIC expressed in µg/mL. Every experiment in the antifungal assay was replicated twice in order to define the MIC values.

RESULTS AND DISCUSSION

A- Chemistry

The novel quinoline derivatives (IV_{a-g}) (V_{1-7}) (VI_{1-7}) were prepared as outlines in scheme 1[16]. The starting materials, 2-aryl-6-substituted-quinoline-4-carboxylic acids I_{a-j} and 2-aryl-6-substituted-quinoline-4-carbonyl chlorides II_{1-7} were prepared as previously reported[17], and then subjected to hydrazinolysis using hydrazine hydrate in refluxing ethanol to afford the reported intermediate acid hydrazides III_{a-g}[17]. Moreover, new 2[(2-aryl-6-substituted-4-quinolyl) carbonyl]-1-hydrazine, carbothiamides (IV_{1-7}) were synthesized in high yields through refluxing 2-aryl-quinoline-4-carbohydrazides (III_{a-g}) with potassium thiocyanate in water containing hydrochloric acid. The novel oxadiazole derivatives V_{a-g} were produced via the reaction of the aforemention, thiosemicarbasides VI_{a-g} and iodine solution under basic condition.

On the other hand, the novel 5-aryl-1,3,4-thiadiazol-2-amines (VI_{a-g}) were prepared via two methods, either through the reaction of 2-aryl-6-substituted quinoline 4-carboxylic acids ($I_{b-d,f,h-j}$) with thiosemicarbazide (method A) or through treatment of thiosemicarbazides ($IV_{b,d,f,g}$) with concentrated sulfuric acid to generate 5-aryl-1,3,4-thiadiazol-2-amines ($VI_{b,d,f,g}$) (method B). The corresponding final compounds ($VI_{b,d,f,g}$) prepared by method B than obtained through method A except for compound VI_d (80% versus 65%).

B- Biology

Antimicrobial activity

The new target oxadiazoles and thiadiazoles were assayed in vitro for antibacterial activity against *Staphylococcus aureus* and *Bacillus subtilis* (examples for Gram-positive bacteria) and *Escherichia coli* and *Salmonella typhimurium* (examples for Gram-negative bacteria) and the antifungal activity was evaluated against *Candida albicans* and *Saccharomyces cerevisiae*.

The MIC values were determined by the two-fold serial dilution technique in Mueller-Hinton broth and sabouraud dextrose broth for the antibacterial and anti-fungal assay, respectively. For comparison, ampicillin was used as the reference antibacterial agent and nystatin was employed as the reference antifungal agent.

The MIC values for test compounds as well as reference standard are given in (Table 4).

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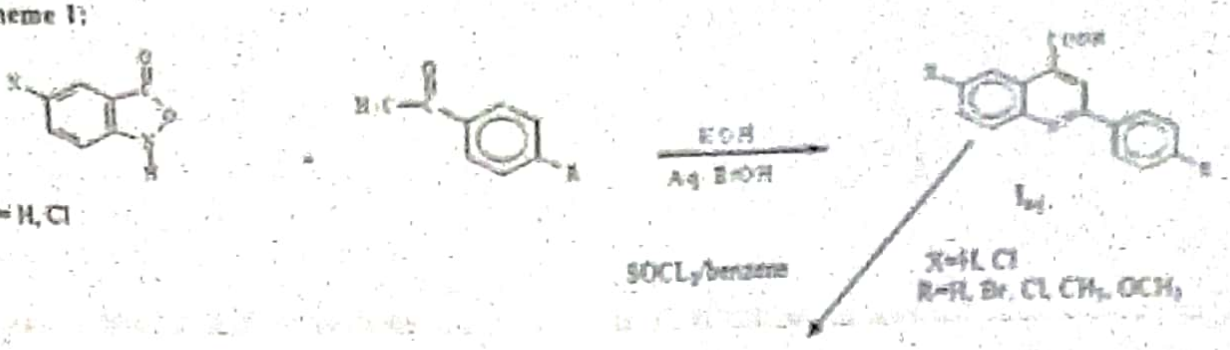
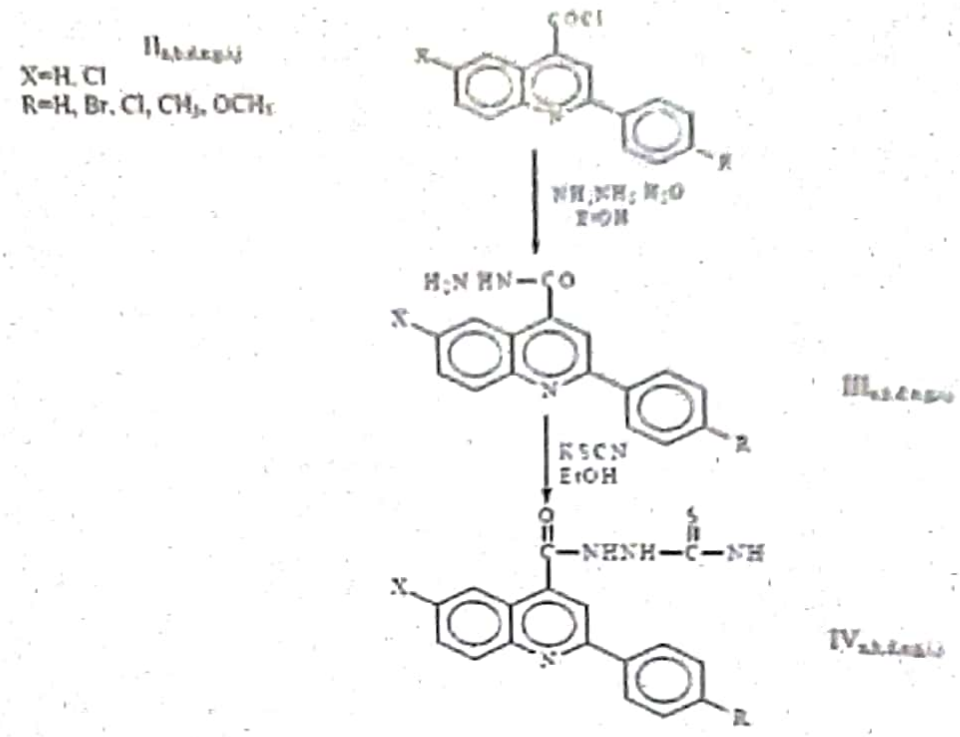
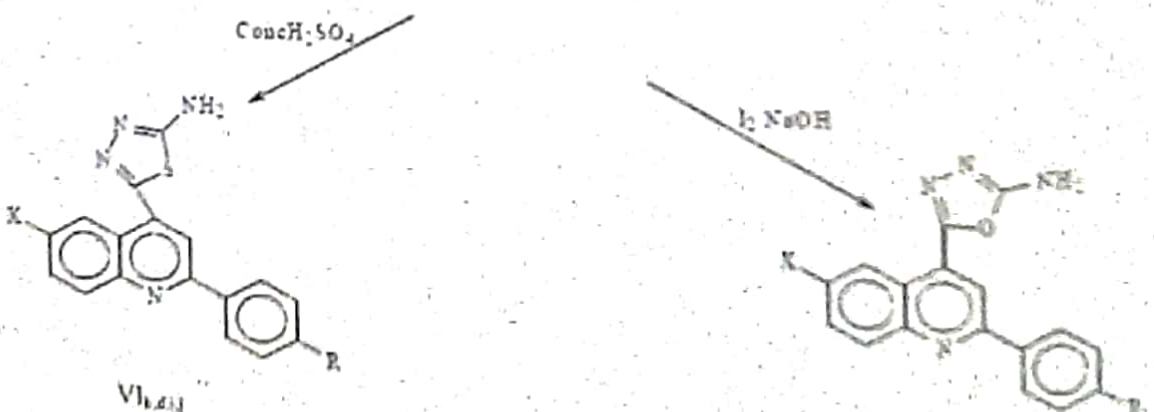
Scheme 1:







Scheme 2:

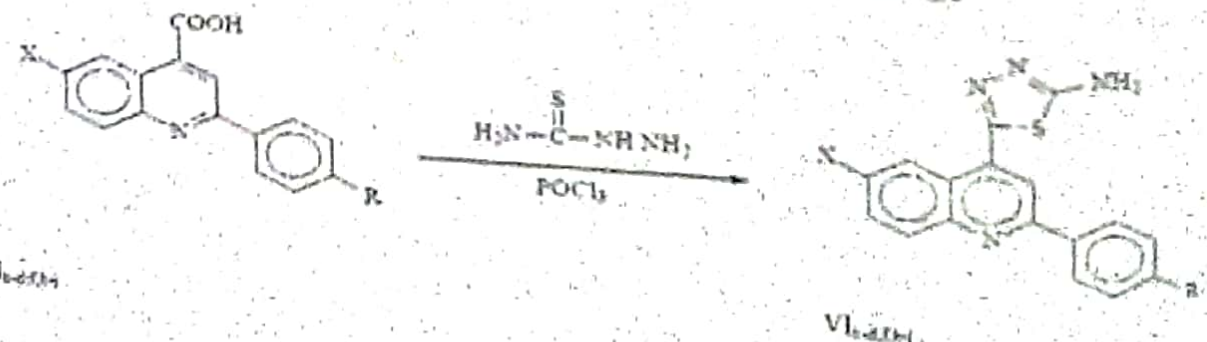


Table (4): MIC values for the target oxadiazoles and thiadiazoles.

	LOG P	MIC (mg/ml)					
		Gram positive bacteria		Gram negative bacteria		Fungi	
		Staph. aureus ATCC25923	*Bacillus subtilis* ATCC	*E. coli* ATCC 10563	*Salmonella typhimurium* NCTC14024	*Candida albicans* ATCC 10231	*Saccharomyces cerveslae* ATCC
V_a	3.36±0.62	>128	>128	>128	>128	>128	>128
V_b	4.1±0.65	>128	>128	>128	>128	>128	16
V_d	3.82±.62	8	>128	>128	>128	>128	>128
V_e	3.17±0.63	>128	>128	>128	>128	>128	>128
V_g	4.75±0.66	16	>128	>128	>128	32	64
V_i	4.46±0.63	>128	>128	>128	>128	>128	16
V_j	3.82±0.64	8	>128	>128	>128	64	64
VI_b	4.69±0.65	8	>128	>128	>128	>128	16
VI_c	4.51±0.63	>128	>128	>128	>128	64	>128
VI_d	4.4±0.63	4	>128	>128	>128	>128	32
VI_f	4.59±0.63	8	>128	>128	>128	>128	>128
VI_h	5.16±.64	4	>128	>128	>128	>128	>128
VI_i	5.05±0.63	>128	>128	>128	>128	>128	16
VI_j	4.4±0.64	16	>128	>128	>128	64	16
Ampicillin		2	2	2	2	-	-
Nystatin		-	-		-	4	4

The obtained results showed that all the testes compounds lacked antibacterial activity against *Bacillus subtilis*, *Escherichia coli* and *Salmonella typhimurium*, while some compounds namely, V_d, V_g, V_g, VI_b, IV_d, IV_f, IV_h, IV_i displayed antibacterial activity against *Staphylococcus aureua*. The 1,3,4-thiadiazoles VI_d and VI_h exhibited the most potent antibacterial activity with MIC values of 4 µg/ml. Furthermore, the results revealed that most of the compounds have antifungal activity against both *Candida albicans* and *Saccharomyces cerevisiae*. The 1,3,4-oxadiazoles V_g and V_j and the 1,3,4-thiadiazoles VI_c and VI_j showed weak activity against *Candida albicans*. On the other hand, nearly half of the tested compounds displayed activity against *Saccharomyces cerevisiae* with MIC values ranging from 16 to 64 µg/ml.

Log P values were calculated for the target compounds using ACD/Log P software and plotted against antibacterial and antifungal activity expressed as –log MIC values as illustrated in Figures 1 and 2. The hydrophobic character of the tested compounds correlated weakly with antibacterial (r = 0.154) and antifungal (r = 0.286) activity.

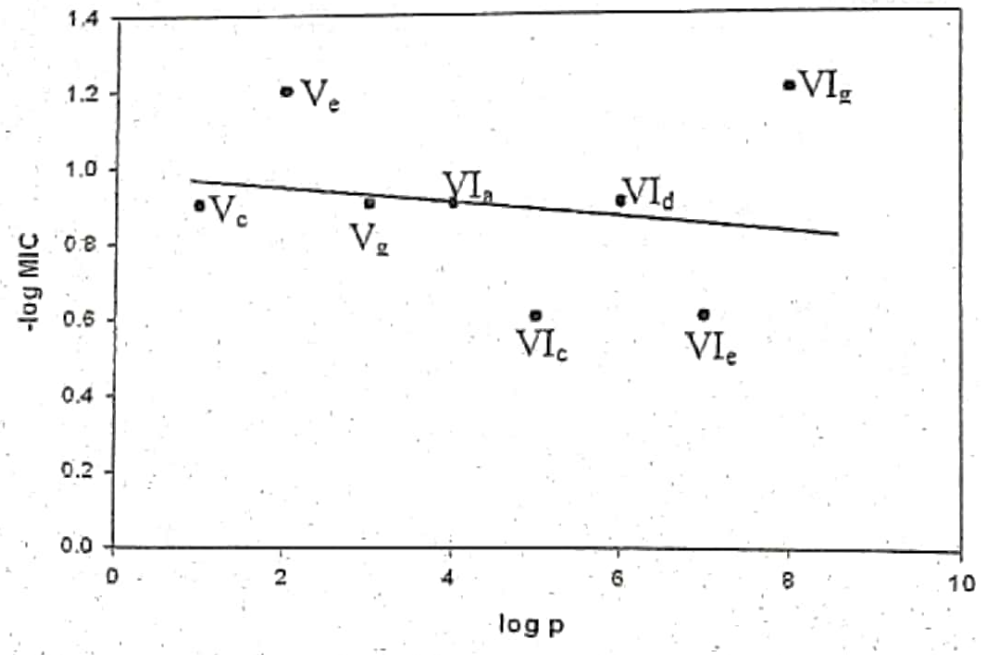


Fig. (1): Correlation between hydrophobicity of the tested compounds and antibacterial activity against *Staphylococcus aureus*.

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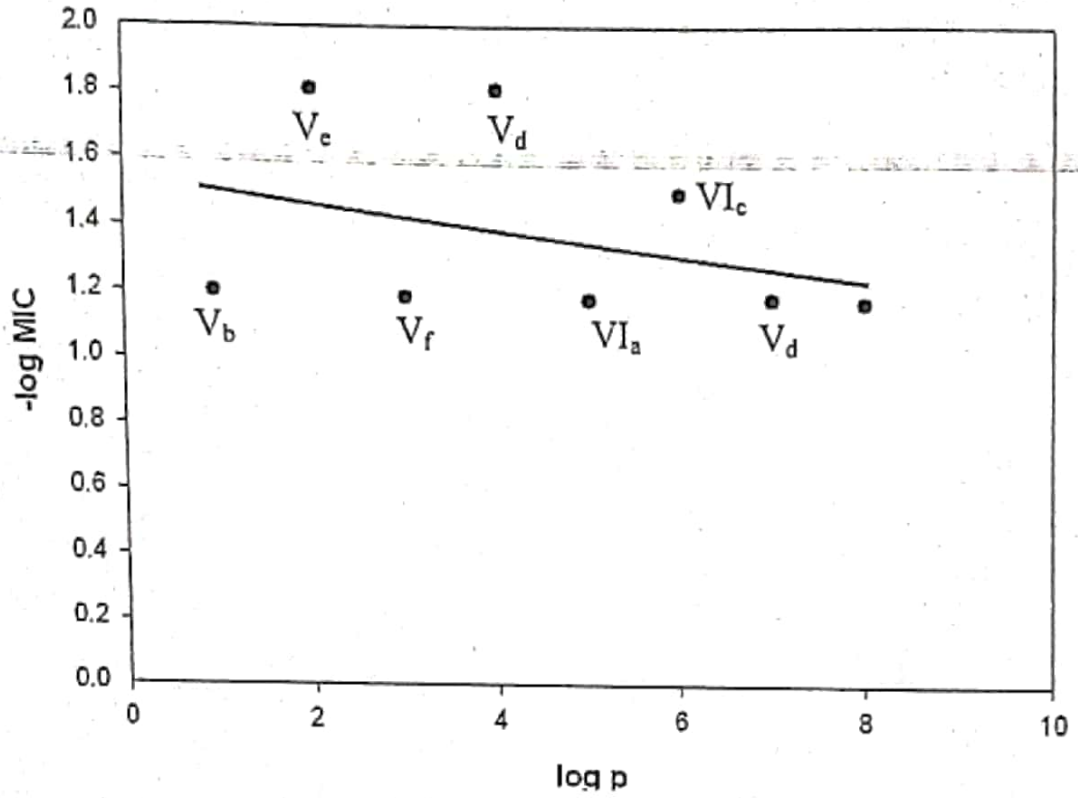

Fig. (2): Correlation between hydrophobicity of the tested compounds and antifungal activity against *Saccharomyces cerevisiae*.

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التشييد والنشاط المضاد للميكروبات لبعض مشتقات الكينولين الجديده

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تم تشييد سلسله جديده من 5-{2-اريل-6-مستدل-4-كينولين}-4,3,1-اوكسادبازول-2-امين (V_{1-7}) من حلقه الوسيط ثيوسيميكاربازات (IV_{a-g}) وكذلك تم تحضير سلسله جديده من 5-{2-اريل-6-مستدل-4-كينولين}-4,3,1-ثيادبازول-2-امين (VI_{a-g}) من خلال حلقه كينولين - 4 – حمض الكربوكسيلك او حلقه ثيوسيميكاربازات وقد تم تقييم فاعليه مشتقات الاوكسادبازول و الثيادبازول ضد البكتيريا موجبه وسالبه الجرام والفطريات.

وقد ظهر من نتائج التقييم ان المركبات VId,h 4,3,1-ثيادبازول ليهما فاعليه عاليه بتركيز 4 ميكروجرام / مل ضد البكتيريا.