Bull. Pharm. Sci., Assiut University, Vol. 28, Part 1, June 2005, pp. 79-93.

SYNTHESIS OF SOME QUINOLINE THIOSEMICARBAZONE DERIVATIVES OF POTENTIAL ANTIMICROBIAL ACTIVITY

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مركبات اليثوسيميكربازون تتميز بأن لها فاعليات بيولوجية مختلفة كمضادات للبكتريا والفطريات والسل وترياق ضد سموم المعادن وذلك اعتماداً على طبيعة المستبدلات على النتروجين رقم ١ ورقم ٤ لجزئية الثيوسيميكربازون إضافة إلى مشتقات ٨ هيدروكسى كينولين وكما هو مدون بالتراث العلمي كمضادات للبكتريا حيث أن لها صفات مخلبية مستمدة من مجموعة ٨ هيدروكسى وذرة النتروجين بحلقة الكينولين.

وتشمل تلك الدراسة تحضير مشتقات جديدة من ٥ استيل (أو ٥ بنزويل) ٨ هيدروكسى كينولين - ٤ مستبدل-ثيوسيميكربازون لاستيضاح تأثير تلك التحورات على النشاط المضاد للبكتريا ، كذلك تم حلقنة بعض الثيوسيميكربازونات للحصول على مشتقات من الثيازولدينون كوسيلة لادخال مجموعة اليثول الخاصة بجزئية الثيوسيميكربازون بداخل حلقة غير متجانسة والهدف من ذلك هو دراسة مدى ما يتأثر به النشاط البيولوجي من جراء أحتواء مجموعة الثيوسيميكربازون في حلقة غير متجانسة. وقد تم اختيار المستبدلات R,R^1 لتعطى قاعة لدراسة نتائج الاختلاف في الخواص الاليكترونية للمركبات المخلقة على النشاط الذي أعطته تلك المركبات. قد تم أثبات التراكيب البنائية للمركبات باستخدام الاشعة تحت الحمراء والرنين النووى المغناطيسي كما تم استخدام طيف الكتلة لبعض المركبات. كما أجرى اختبار الفاعلية البيولوجية للمركبات المشيدة كمضادات للبكتريا والفطريات بالمقارنة مع عقار الاستربتومايسين كمضاد للبكتريا وعقار كلوتريمازول كمضاد للفطريات باستخدام طريقة cup inhibition zone test .

*5-Acetyl (or 5-benzoyl)-8-hydroxyquinoline-4-substituted thiosemi- carbazones (**IIa-m, IIIa-m** respectively) have been prepared via the condensation of 5-acetyl (or 5-benzoyl)-8-hydroxyquinoline with the appropriate 4-substituted-3-thiosemicabazides (**Ia-l**). The thiosemicarbazones (**IIa-l, IIIa-f**) were subjected to cyclization into the corresponding thiazolidinones (**IVa-l, Va-f**) by the reaction with ethyl bromoacetate in the presence of anhydrous sodium acetate. The structures of the thiosemicarbazones as well as the corresponding thiazolidinones were assigned based on both elemental and spectroscopic evidences. The prepared compounds were also evaluated for antibacterial and antifungal activities.*

INTRODUCTION

Thiosemicarbazones, a class of compounds possessing a wide spectrum of numerous pharmacological activities, have been studied for activity as antibacterial,[1-6] antifungal,[7-9] antituberculous,[10-13] anti-malarial,[14-17] antiviral infection,[18-21] as well as analgesic and antipyretic.[22] In the past few years, thiosemicarbazones have been of great interest because of their reported antitumor activity.[23-34] In addition, thiosemicarbazones were reported as antidotal for metals toxicity.[35-36] In a search for new biologically active agents, many research workers have successfully synthesized a variety of different aromatic and heteroaromatic thiosemi-carbazone derivatives. This depending on the

Received in 7/11/2004 & Accepted in 30/1/2005

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nature of the substituents at N^1 and N^4 of the thiosemicarbazone moiety. In addition 8-hydroxyquinoline and its derivatives were reported as antimicrobial agents.[37] The antimicrobial activity has been attributed to the chelating properties provided by the 8-hydroxy group and quinoline ring nitrogen.[38] In the present investigation, it was of interest to prepare new 5-acetyl (or 5-benzoyl)-8-hydroxyquinoline-4-substituted thiosemi-carbazone derivatives, in which thiosemi-carbazone moiety incorporated with 8-hydroxyquinoline nucleus to explore this interesting modifications for the development of potential antimicrobial activity. Thiosemi-carbazones were then cyclized into thiazolidinone ring systems as a mean of trapping the SH function of thiosemicarbazone moiety within a heterocyclic ring. This was performed to study the effect on the activity of the product when the thiosemicarbazones are encaged in a rigid heterocyclic structure.

EXPERIMENTAL

Materials and equipments

Melting points were determined on an electrothermal melting point apparatus (Stuart Scientific Co.) and were uncorrected. Elemental microanalyses were performed on Perkin-Elmer, 240° Elemental Analyzer, at the Faculty of Science, Assiut University. ^{1}H-NMR spectra were run on Varain Em-360L NMR spectrophotometer (60 MHz) (Varian USA) at the Faculty of Pharmacy, Assiut University, and on Joel, Lambda, Oxford NMR YH (400MHz, Japan) at Assiut University Central Lab using tetramethylsilane (TMS) as an internal standard. The chemical shifts are expressed in δ (ppm). IR spectra were carried out as KBr disc on Shimadzue Infrared Spectrophotometer 200-91527 at the Faculty of Pharmacy, Assiut University. Mass spectra were performed with JEOL JMS600, Assiut Uni-versity Central Lab, Assiut and at the Microanalytical center, Faculty of Science, Cairo University. The reported procedure for the synthesis of 5-acetyl (or 5-benzoyl)-8-hydroxyquinoline were utilized,[39] also 4-substituted-3-thiosemicarbazide compounds (Ia-l) were prepared according to reported method.[14]

Synthesis of 5-acetyl (or 5-benzoyl)-8-hydroxyquinoline-4-substituted thiosemi-carbazone compounds (IIa-m, and IIIa-m)

A mixture of thiosemicarbazide or appropriate 4-substituted-3-thiosemi-carbazide (5.3 mmol) and 5-acetyl (or 5-benzoyl)-8-hydroxyquinoline (5.3 mmol) in 50 ml absolute ethanol containing 4 drops conc. HCl was heated under reflux for 2-8 hr. The precipitate formed directly or after addition of water for compounds IIb, IIc, IId, IIe, IIf was filtered, dried and crystallized from suitable solvent. The yields, melting points and elemental microanalyses were listed in Tables 1, 3. The ^{1}H-NMR data were listed in Tables 2, 4.

Synthesis of 5-acetyl (or 5-benzoyl)-8-hydroxyquinoline 2-(3-substituted-4-oxo-thiazolidin-2-ylidene) hydrazone compounds (IVa-l&Va-f)

A solution of 5-acetyl (or 5-benzoyl)-8-hydroxyquinoline-4- substituted thiosemi-carbazones (1.5 mmol) in absolute ethanol (30ml) was treated with equimolar amount of ethyl bromoacetate (1.5 mmol, 0.166 ml) in presence of anhydrous sodium acetate (100 mg). The reaction mixture was heated under reflux for 4-6 h then concentrated and left over night. The formed crystals were filtered and recrystallized from absolute ethanol. The yield, melting point and elemental microanalyses were listed in Tables 5, 7. The ^{1}H-NMR data were listed in Tables 6, 8.

Antimicrobial activity (organisms and culture conditions)

Material and method

Antimicrobial activity of the synthesized compounds **IIa-m**, **IIIa-m**, **IVa-j** and **Va-f** were tested against:

a) Bacteria

Gram-positive bacteria: *Micrococcus luteus,* and *Staphylococcus aureus.* Gram-negative bacteria: *Pseudomononus aeroginosa* and *Serratia marscens.*

b)Fungi

Candida albicans, Trichophyton rubrum, Geotrichum candidum,and Scopulariopsis brivicalis.

Table 1: Physical data of 5-acetyl-8-hydroxyquinoline-4-substituted thiosemicarbazone compounds **(II a-m)**.

No.	R^1	Yield %	M.P° Solvent of crys.	M.F/ M.Wt	Microanalysis Calculated/found			
					C %	H %	N %	S%
IIa	H	86	222-24 E	$C_{12}H_{12}N_4OS$ 260.32	55.37 54.33	4.65 4.76	21.52 21.26	12.32 12.27
IIb	CH_3	81	163-65 E/W	$C_{14}H_{15}N_3OS$ 274.34	56.91 56.98	5.14 4.51	20.42 20.41	11.69 12.09
IIc	C_2H_5	85	140-42 E/W	$C_{14}H_{16}N_4OS$ 288.37	58.31 58.15	5.59 5.88	19.43 19.54	11.12 11.29
IId	$CH_2CH{=}CH_2$	86	142-44 E/W	$C_{15}H_{16}N_4OS$ 300.38	59.98 59.79	5.37 5.47	18.6 18.65	10.68 10.87
IIe	C_4H_9(n)	79	130-32 E/W	$C_{16}H_{20}N_4OS$ 316.42	60.73 60.72	6.37 5.85	17.71 17.67	10.13 9.83
IIf	C_6H_{11} (c)	87	185-87 E/W	$C_{18}H_{22}N_4OS$ 342.46	63.13 62.81	6.48 6.98	16.36 16.23	9.36 9.37
IIg	C_6H_5	83	215-17 E	$C_{18}H_{16}N_4OS$ 336.41	64.26 63.99	4.79 4.90	16.65 16.73	9.53 9.76
IIh	o-CH_3-C_6H_4	75	210-12 E	$C_{19}H_{18}N_4OS$ 350.44	65.12 64.76	5.18 5.24	15.99 15.94	9.15 8.83
IIi	m-CH_3-C_6H_4	63	140-42 E	$C_{19}H_{18}N_4OS$ 350.44	65.12 64.74	5.18 4.66	15.99 15.96	9.15 9.01
IIj	p-CH_3-C_6H_4	65	220-22 E	$C_{19}H_{18}N_4OS$ 350.44	65.12 64.36	5.18 4.71	15.99 16.05	9.15 9.22
IIk	p-OCH_3-C_6H_4	77	158-60 E	$C_{19}H_{18}N_4O_2S$ 366.44	62.28 62.06	4.95 5.10	15.29 15.32	8.75 8.60
IIl	p-F-C_6H_4	79	147-49 E	$C_{18}H_{15}FN_4OS$ 354.40	61.00 60.43	4.27 4.18	15.81 15.78	9.05 8.67
IIm	o-Cl-C_6H_4	75	195-97 E	$C_{18}H_{15}ClN_4OS$ 379.86*	56.92 57.14	3.98 4.10	14.75 14.64	8.44 7.42

* Contain 0.5 molecule of water

E: Ethanol

E/W: Ethanol/Water (2:1)

Table 2: ^{1}H-NMR data of 5-acetyl-8-hydroxyquinoline-4-substituted thiosemicarbazone compounds **(II a-m)**.

No.	R^1	^{1}H NMR (δ ppm in $CDCl_3$)*
IIa	H	10.23 (s, 1H, N^2HCS); 8.90 (d, 1H, H_2 of quinoline); 8.80 (d, 1H, H_4 of quinoline); 8.40-7.36 (m, 3H, OH, $H_{3,6}$ of quinoline); 7.10 (d, 1H, H_7 of quinoline); 4.13 (br. s, 2H, NH_2); 2.43, 2.33 (2s, 3H, CH_3); [80%, 20%]**
IIb	CH_3	9.23 (br. s, 1H, N^2HCS); 9.13 (d, 1H, H_2 of quinoline); 8.96 (d, 1H, H_4 of quinoline); 8.63 (br. s, 1H, OH); 8.26-7.63 (m, 3H, $N^4\underline{H}CH_3$, $H_{3,6}$ of quinoline); 7.45 (d, 1H, H_7 of quinoline); 3.33 (d, 3H, $NHC\underline{H}_3$); 2.48, 2.45 (2s, 3H, CH_3) [65%, 35%]
IIc	C_2H_5 ***	9.20 (br. s, 1H, N^2HCS); 8.70 (d, 1H, H_2 of quinoline); 8.56 (d, 1H, H_4 of quinoline); 7.94 (s, 1H, OH); 7.59 (d, 1H, H_6 of quinoline); 7.55-6.89 (m, 3H, $N^4\underline{H}CH_2$, $H_{3,7}$ of quinoline); 3.42 (m, 2H, $C\underline{H}_2CH_3$); 2.19, 2.09 (2s, 3H, CH_3) [60%, 40%]; 1.02, 0.94 (2t, 3H, $CH_2C\underline{H}_3$) [60%, 40%]
IId	$CH_2CH=CH_2$	9.23 (br. s, 1H, N^2HCS); 9.10 (d, 1H, H_2 of quinoline); 8.90 (d, 1H, H_4 of quinoline); 8.60-7.70 (m, 4H, OH, $N^4\underline{H}CH_2$, $H_{3,6}$ of quinoline); 7.34 (d, 1H, H_7 of quinoline); 6.50-5.80 (m, 1H, $C\underline{H}=CH_2$); 5.46 (d, 1H, $CH=C\underline{H}_2$); 5.21 (d, 1H, $CH=C\underline{H}_2$); 4.50 (t, 2H, $NHC\underline{H}_2$); 2.53, 2.45 (2s, 3H, CH_3); [60%, 40%]
Iie	C_4H_9 (n)	9.25 (br. s, 1H, N^2HCS); 9.16-8.80(m, 2H, $H_{2,4}$ of quinoline); 8.50 (br. s, 1H, OH); 8.10-7.25 (m, 4H, $N^4\underline{H}CH_2$, $H_{3,6,7}$ of quinoline); 3.80 (q, 2H, $NHC\underline{H}_2$); 2.50, 2.41 (2s, 3H, CH_3) [73%, 27%]; 2.00-1.16 (m, 4H, $C\underline{H}_2C\underline{H}_2CH_3$); 1.10-0.70 (t, 3H, $CH_2C\underline{H}_3$)
IIf	C_6H_{11}(c)	9.00-8.60 (m, 3H, N^2HCS, $H_{2,4}$ of quinoline); 8.20 (s, 1H,OH); 8.06-7.10 (m, 4H, $N^4\underline{H}$, $H_{3,6,7}$ of quinoline) 4.60-4.00 (m, 1H, $NHC\underline{H}$ of cyclohexyl); 2.40, 2.35 (2s, 3H, CH_3) [60%, 40%]; 2.30-0.90 (m, 10H, $(C\underline{H}_2)_5$ of cyclohexyl)
IIg	C_6H_5***	10.64, 10.18 (2s, 1H, N^2HCS) [83%, 17%]; 9.84, 9.24 (2s, 1H,$N^4\underline{H}$phenyl), [83%, 17%]; 8.86 (d, 1H, H_2 of quinoline); 8.68 (d, 1H, H_4 of quinoline); 7.67-6.09(m, 9H, OH, $H_{3,6,7}$ of quinoline, $NHC_6\underline{H}_5$); 2.49, 2.38 (2s, 3H, CH_3) [83% 17%]**
IIh	o-CH_3-C_6H_4	10.95, 10.26 (2s, 1H, N^2HCS) [80%, 20%]; 9.90, 9.40 (2s, 1H,$N^4\underline{H}$-o.tolyl) [80%, 20%]; 9.30-8.90 (m, 2H, $H_{2,4}$ of quinoline); 8.15-7.15 (m, 8H, OH, $H_{3,6,7}$ of quinoline, $NHC_6\underline{H}_4$); 2.63 (s, 3H, CH_3 of o.tolyl); 2.45, 2.30 (2s, 3H, CH_3) [80% 20%]**
IIi	m-CH_3-C_6H_4	9.72 (br. S, 1H, N^2HCS); 9.60 (br. S, 1H, $N^4\underline{H}$- m.tolyl); 9.33-8.83 (m, 2H, $H_{2,4}$ of quinoline); 8.60 (br. S, 1H, OH); 8.2 (d, 1H, H_6 of quinoline); 7.96-7.06 (m, 6H, $H_{3,7}$ of quinoline, $NHC_6\underline{H}_4$); 2.63 (s, 3H, CH_3 of m.tolyl); 2.60, 2.50 (2s, 3H,CH_3) [60%, 40%]
IIj	p-CH_3-C_6H_4	9.66, 9.54 (2s, 1H, NH^2CS) [60%, 40%]; 9.26 (br. S, 1H, $N^4\underline{H}$-p.tolyl); 9.10-8.80 (m, 2H, $H_{2,4}$ of quinoline); 8.63 (br. S, 1H, OH); 8.17 (d, 1H, H_6 of quinoline); 7.96-7.23 (m, 6H, $H_{3,7}$ of quinoline, $NHC_6\underline{H}_4$); 2.6 (s, 3H, CH_3 of p. tolyl); 2.50, 2.40 (2s, 3H,CH_3) [60%, 40%]
IIk	p-CH_3O-C_6H_4	9.52, 9.42 (2s, 1H, NH^2CS) [75%, 25%]; 9.25 (br. S, 1H, $N^4\underline{H}$-p.methoxyphenyl); 9.12-8.70 (m, 2H, $H_{2,4}$ of quinoline); 8.52 (br. S, 1H, OH); 8.10 (d, 1H, H_6 of quinoline); 7.92-6.86 (m, 6H, $H_{3,7}$ of quinoline, $NHC_6\underline{H}_4$); 3.86 (s, 3H, OCH_3); 2.53, 2.43 (2s, 3H,CH_3); [75%, 25%]
IIl	p-F-C_6H_4	11.06, 10.53 (2s, 1H, N^2HCS) [80%, 20%]; 10.13 (s, 1H, $N^4\underline{H}$-p. fluorophenyl); 9.30-8.80 (m, 2H, $H_{2,4}$ of quinoline); 8.36-7.06 (m, 8H, OH, $H_{3,6,7}$ of quinoline, $NHC_6\underline{H}_4$); 2.66, 2.55 (2s, 3H, CH_3) [80% 20%]**
IIm	o-Cl-C_6H_4	10.23, 10,10 (2s, 1H, N^2HCS) [60%, 40%]; 9.33-8.73 (m, 3H, $N^4\underline{H}$-o.chlorophenyl, $H_{2,4}$ of quinoline); 8.62 (br. S, 1H, OH); 8.20 (d, 1H, H_6 of quinoline); 7.96-7.03 (m, 6H, $H_{3,7}$ of quinoline, $NHC_6\underline{H}_4$); 2.80, 2.70 (2s, 3H,CH_3) [60%, 40%]**

*Protons of NH, NH_2 and OH groups are exchangeable by D_2O
** d_6-DMSO: dimethylsulfoxide
*** 400 MHz

Table 3: Physical data of 5-benzoyl-8-hydroxyquinoline-4-substituted thiosemicarbazone compounds **(III a-m)**.

No.	R^1	Yield %	M.P° Solvent of crys.	M.F/ M. Wt	Microanalysis Calculated/found			
					C %	H %	N %	S %
IIIa	H	81	245-47 E	$C_{17}H_{14}N_4OS$ 322.39	63.33 63.39	4.38 4.57	17.38 17.24	9.95 9.84
IIIb	CH_3	82	263-65 E	$C_{19}H_{17}N_3OS$ 345.41*	62.59 63.08	4.67 3.87	16.22 16.65	9.28 9.79
IIIc	C_2H_5	85	238-40 E	$C_{19}H_{18}N_4OS$ 350.44	65.12 65.02	5.18 5.44	15.99 16.05	9.15 8.88
IIId	$CH_2CH=CH_2$	72	218-20 E/W	$C_{20}H_{18}N_4OS$ 362.45	66.28 66.19	5.01 4.98	15.46 15.48	8.85 8.53
IIIe	C_4H_9(n)	79	165-67 E/W	$C_{21}H_{22}N_4OS$ 378.49	66.64 66.47	5.86 6.32	14.80 14.83	8.47 8.30
IIIf	C_6H_{11} (c)	77	240-42 E	$C_{23}H_{24}N_4OS$ 404.53	68.29 68.08	5.98 6.58	13.85 13.85	7.93 8.34
IIIg	C_6H_5	71	185-87 E	$C_{23}H_{18}N_4OS$ 398.48	69.32 69.26	4.55 4.12	14.06 13.57	8.05 7.87
IIIh	o-CH_3-C_6H_4	75	205-07 E	$C_{24}H_{20}N_4OS$ 412.51	69.88 69.62	4.89 4.18	13.58 13.58	7.77 7.90
IIIi	m-CH_3-C_6H_4	77	180-82 E	$C_{24}H_{20}N_4OS$ 412.51	69.88 58.80	4.89 4.46	13.58 13.19	7.77 7.68
IIIj	p-CH_3-C_6H_4	79	195-97 E	$C_{24}H_{20}N_4OS$ 412.51	69.88 69.12	4.89 5.47	13.58 13.51	7.77 7.75
IIIk	p-OCH_3-C_6H_4	65	120-22 E	$C_{24}H_{20}N_4O_2S$ 437.51	65.89 66.00	4.84 5.03	12.80 12.65	7.33 7.17
IIIl	p-F-C_6H_4	68	225-27 E	$C_{23}H_{17}FN_4OS$ 416.47	66.33 65.40	4.11 3.81	13.45 13.84	7.70 7.83
IIIm	o-Cl-C_6H_4	67	182-84 E	$C_{23}H_{17}ClN_4OS$ 450.93**	61.26 59.57	3.80 3.65	12.42 14.39	7.11 7.69

* Contain 0.5 molecule of water

** Contain one molecule of water

E: Ethanol

E/W: Ethanol/Water (2:1)

Table 4: ^{1}H-NMR data of 5-benzoyl-8-hydroxyquinoline-4-substituted thiosemicarbazone compounds **(III a-m)**.

No	R^1	^{1}H NMR (δ ppm in $CDCl_3$)*
IIIa	H	9.13 (d, 1H, H_2 of quinoline); 8.96 (br. s, 1H,N^2HCS); 8.5 (br. s, 1H,OH); 8.2-7.4 (m, 11H, $H_{3,4,6,7}$ of quinoline, C-Ph, NH_2)
IIIb	CH_3	9.16 (d, 1H, H_2 of quinoline); 8.6 (br. s, 1H, OH); 8.93-8.60 (br. m, 2H, OH, N^2HCS); 8.3-7.5 (m, 10H, $H_{3,4,6,7}$ of quinoline, C-Ph, $N^4\underline{H}CH_3$); 3.3 (d, 3H, $NHC\underline{H}_3$)
IIIc	C_2H_5***	8.83 (dd, 1H, H_2 of quinoline); 8.41 (br. s, 1H, OH); 7.75 (dd, 1H, H_4 of quinoline); 7.70 (br. s, 1H, N^2HCS); 7.48-7.24 (m, 9H, $H_{3,6,7}$ of quinoline, C-Ph, $N^4\underline{H}CH_2$); 3.77 (m, 2H, $C\underline{H}_2CH_3$); 1.34 (t, 3H, $CH_2C\underline{H}_3$)
IIId	$CH_2CH=CH_2$	9.0 (d, 1H, H_2 of quinoline); 8.6 (br. S, 1H, OH); 8.2-7.23 (m, 11H, N^2HCS, $H_{3,4,6,7}$ of quinoline, C-Ph, $N^4\underline{H}CH_2$); 6.56-5.83 (m, 1H, $C\underline{H}=CH_2$); 5.46 (t, 2H, $CH=C\underline{H}_2$); 4.5 (t, 2H, $NHC\underline{H}_2$)
IIIe	C_4H_9 (n)	9.15 (d, 1H, H_2 of quinoline); 8.76 (br. s, 1H, OH); 8.30-7.40 (m, 11H, N^2HCS, $H_{3,4,6,7}$ of quinoline, C-Ph, $N^4\underline{H}CH_2$); 3.90 (q, 2H, $NHC\underline{H}_2$); 2.10-1.30 (m, 4H, $C\underline{H}_2C\underline{H}_2CH_3$); 1.10 (t, 3H, $CH_2C\underline{H}_3$)
IIIf	C_6H_{11}(c)	9.00 (d, 1H, H_2 of quinoline); 8.56 (br. s, 1H, OH); 8.20-7.20 (m, 11H, N^2HCS, $H_{3,4,6,7}$ of quinoline, C-Ph, $N^4\underline{H}$-cyclohexyl); 4.80-4.06 (m, 1H, $NHC\underline{H}$ of cyclohexyl); 2.56-1.00 (m, 10H, $(C\underline{H}_2)_5$ of cyclohexyl)
IIIg	C_6H_5	10.2 (br. s, 1H, N^2HCS); 9.15(d, 1H, H_2 of quinoline); 8.96 (br. s, 1H, OH); 8.20-7.10 (m, 15H, $N^4\underline{H}$-phenyl, $H_{3,4,6,7}$ of quinoline, C-Ph, $NHC_6\underline{H}_5$)
IIIh	o-CH_3-C_6H_4	9.66 (br. s, 1H, N^2HCS); 9.15(d, 1H, H_2 of quinoline); 8.95 (br. s, 1H, OH); 8.30-7.10 (m, 14H, $N^4\underline{H}$- o.tolyl, $H_{3,4,6,7}$ of quinoline, C-Ph, $NHC_6\underline{H}_4$); 2.56 (s, 3H, CH_3 of o.tolyl).
IIIi	m-CH_3-C_6H_4	10.65 (br. s, 1H, N^2HCS); 9.50 (br. s, 1H, $N^4\underline{H}$-m.tolyl); 9.20 (d, 1H, H_2 of quinoline); 8.20-6.90(m, 14H, OH, $H_{3,4,6,7}$ of quinoline, C-Ph, NH $C_6\underline{H}_4$); 2.56 (s, 3H, CH_3 of m.tolyl)**
IIIj	p-CH_3-C_6H_4	9.7 (br. s, 1H, N^2HCS); 9.06 (d, 1H, H_2 of quinoline); 8.83 (s, 1H, OH); 8.56-7.20 (m, 14H, $N^4\underline{H}$- p.tolyl, $H_{3,4,6,7}$ of quinoline, C-Ph, $NHC_6\underline{H}_4$); 2.43 (s, 3H, CH_3 of p. tolyl)
IIIk	p-CH_3O-C_6H_4	9.93 (br. s, 1H, N^2HCS); 9.63 (br. s, 1H, $N^4\underline{H}$-p.methoxyphenyl); 9.16 (d, 1H, H_2 of quinoline); 8.10-6.86 (m, 14H, OH, $H_{3,4,6,7}$ of quinoline, C-Ph, NH $C_6\underline{H}_4$); 3.90 (s, 3H, OCH_3)**
IIIl	p-F-C_6H_4	10.15 (br. s, 1H, N^2HCS); 9.95(br. s, 1H, $N^4\underline{H}$- p.fluorophenyl); 9.20 (d, 1H, H_2 of quinoline); 8.10-7.10 (m, 14H, OH, $H_{3,4,6,7}$ of quinoline, C-Ph, NH $C_6\underline{H}_4$)**
IIIm	o-Cl-C_6H_4	10.80 (br. s, 1H, N^2HCS); 10.13 (br. s, 1H, $N^4\underline{H}$- o. chlorophenyl); 9.65 (br. S, 1H, OH); 9.20 (d, 1H, H_2 of quinoline); 8.60 (d, 1H, H_4 of quinoline) 8.25-7.00 (m, 12H, OH, $H_{3,6,7}$ of quinoline, C-Ph, $NHC_6\underline{H}_4$)**

* Protons of NH, NH_2 and OH groups are exchangeable by D_2O
** d_6-DMSO: dimethylsulfoxide
*** 400 MHz

Table 5: Physical data of 5-acetyl-8-hydroxyquinoline-2-(3-substituted-4-oxothiazolidin-2-ylidene) hydrazone compounds **(IV a-l)**.

No.	R^1	Yield %	M.P°	M.F/ M.Wt	Microanalysis Calculated/found			
					C %	H %	N %	S %
IVa	H	58	243-45	$C_{14}H_{12}N_4O_2S$	54.40	3.91	18.12	10.60
				309.34*	53.54	3.41	17.85	10.37
IVb	CH_3	61	270-72	$C_{15}H_{14}N_4O_2S$	57.31	4.49	17.82	10.20
				314.36	58.80	4.35	18.27	10.84
IVc	C_2H_5	79	165-67	$C_{16}H_{16}N_4O_2S$	58.52	4.91	17.06	9.76
				328.39	58.32	5.04	17.03	9.58
IVd	$CH_2CH=CH_2$	70	178-80	$C_{17}H_{16}N_4O_2S$	59.98	4.74	16.46	9.42
				340.40	59.41	4.72	16.44	9.43
IVe	C_4H_9(n)	71	165-67	$C_{18}H_{20}N_4O_2S$	60.65	5.66	15.72	9.00
				356.44	60.45	5.20	15.74	9.39
IVf	C_6H_{11} (c)	63	237-39	$C_{20}H_{22}N_4O_2S$	62.80	5.80	14.65	8.38
				382.48	62.50	5.36	14.59	8.53
IVg	C_6H_5	65	247-49	$C_{20}H_{16}N_4O_2S$	63.81	4.28	14.88	8.52
				376.43	63.58	3.40	14.86	8.775
IVh	o-CH_3-C_6H_4	63	230-32	$C_{21}H_{18}N_4O_2S$	64.60	4.65	14.35	8.21
				390.46	63.98	3.79	14.31	8.69
IVi	m-CH_3-C_6H_4	58	210-12	$C_{21}H_{18}N_4O_2S$	64.60	4.65	14.35	8.21
				390.46	63.85	4.89	14.34	8.03
IVj	p-CH_3-C_6H_4	60	250-52	$C_{21}H_{18}N_4O_2S$	64.60	4.65	14.35	8.21
				390.46	64.06	3.99	14.28	8.34
IVk	p-OCH_3-C_6H_4	68	221-223	$C_{21}H_{18}N_4O_3S$	62.05	4.46	13.78	7.89
				406.46	61.26	4.55	13.75	7.90
IVl	p-F-C_6H_4	66	205-210	$C_{20}H_{15}FN_4O_2S$	60.90	3.83	14.20	8.13
				394.42	59.98	3.72	14.06	8.23

* contain 0.5 molecule of water

Table 6: ^{1}H-NMR data of 5-acetyl-8-hydroxyquinoline-2-(3-substituted-4-oxothiazolidin-2-ylidene) hydrazone compounds **(IVa-l)**.

No	R^1	^{1}H NMR (δ ppm in $CDCl_3$)*
IVa	H	9.57 (d, 1H, H_2 of quinoline); 9.10 (d, 1H, H_4 of quinoline); 8.20-7.30 (m, 4H, OH, $H_{3,6,7}$ of quinoline); 5.36 (br. s, 1H, NH); 3.90 (s, 2H, C$\underline{H}_2$ of thiazolidinone); 2.60 (s, 3H, CH_3)
IVb	CH_3	9.98 (d, 1H, H_2 of quinoline); 9.30 (d, 1H, H_4 of quinoline); 8.30-7.30 (m, 4H, OH, $H_{3,6,7}$ of quinoline); 4.06 (s, 2H, C$\underline{H}_2$ of thiazolidinone); 3.33 (s, 3H, NCH_3); 2.56 (s, 3H, CH_3)
IVc	C_2H_5	9.56 (d, 1H, H_2 of quinoline); 9.00 (d, 1H, H_4 of quinoline); 8.23 (br. S, 1H, OH); 7.99 (d, 1H, H_6 of quinoline); 7.61 (dd, 1H, H_3 of quinoline); 7.40 (d, 1H, H_7 of quinoline); 4.00 (q, 2H, C$\underline{H}_2$$CH_3$); 3.90 (s, 2H, C$\underline{H}_2$ of thiazolidinone); 2.66 (s, 3H, CH_3); 1.30 (t 3H, CH_2C$\underline{H}_3$)
IVd	$CH_2CH=CH_2$	9.50 (d, 1H, H_2 of quinoline); 8.90 (d, 1H, H_4 of quinoline); 7.90-7.20 (m, 4H, OH, $H_{3,6,7}$ of quinoline); 6.40-5.80 (m, 1H, C$\underline{H}$=CH_2) 5.46 (t, 2H, CH=C$\underline{H}_2$); 4.60 (d, 2H, NCH_2); 2.86 (s, 2H, C$\underline{H}_2$ of thiazolidinone); 2.63 (s 3H, CH_3)
IVe	C_4H_9 (n)	9.50 (d, 1H, H_2 of quinoline); 8.90 (d, 1H, H_4 of quinoline); 7.90-7.25 (m, 4H, OH, $H_{3,6,7}$ of quinoline); 4.00 (t, 2H, NCH_2); 3.80 (s, 2H, C$\underline{H}_2$ of thiazolidinone); 2.60 (s, 3H, CH_3); 2.10-1.20 (m, 4H, C$\underline{H}_2$C$\underline{H}_2$CH3)) 1.00 (t, 3H, CH_2C$\underline{H}_3$)
IVf	C_6H_{11}(c)	9.70 (d, 1H, H_2 of quinoline); 9.30 (d, 1H, H_4 of quinoline); 8.20-7.40 (m, 4H, OH, $H_{3,6,7}$ of quinoline); 4.50-4.16 (m, 1H, NC$\underline{H}$ of cyclohexyl); 4.00 (s, 2H, C$\underline{H}_2$ of thiazolidinone); 2.60 (s, 3H, CH_3); 2.50–1.00 (m, 10H, (C$\underline{H}_2$)$_5$ of cyclohexyl)
IVg	C_6H_5	9.60 (d, 1H, H_2 of quinoline); 9.10 (d, 1H, H_4 of quinoline); 8.10-7.30 (m, 9H, OH, $H_{3,6,7}$ of quinoline, NC_6H_5); 4.10 (s, 2H, C$\underline{H}_2$ of thiazolidinone); 2.50 (s, 3H, CH_3)
IVh	o-CH_3-C_6H_4	9.40 (d, 1H, H_2 of quinoline); 8.90 (d, 1H, H_4 of quinoline); 8.30-7.00 (m, 8H, OH, $H_{3,6,7}$ of quinoline, NC_6H_4); 4.00 (s, 2H, C$\underline{H}_2$ of thiazolidinone); 2.33 (s, 3H, CH_3); 2.26 (s, 3H, CH_3 of o.tolyl)
IVi	m-CH_3-C_6H_4	9.50 (d, 1H, H_2 of quinoline); 9.00 (d, 1H, H_4 of quinoline); 8.00-7.20 (m, 8H, OH, $H_{3,6,7}$ of quinoline, NC_6H_4); 4.10 (s, 2H, C$\underline{H}_2$ of thiazolidinone); 2.53 (s, 3H, CH_3); 2.46 (s, 3H, CH_3 of m.tolyl)
IVj	p-CH_3-C_6H_4	9.43 (d, 1H, H_2 of quinoline); 8.90 (d, 1H, H_4 of quinoline); 7.96-7.16 (m, 8H, OH, $H_{3,6,7}$ of quinoline, NC_6H_4); 4.03 (s, 2H, C$\underline{H}_2$ of thiazolidinone); 2.50 (s, 3H, CH_3); 2.43 (s, 3H, CH_3 of p.tolyl)
IVk	p-OCH_3-C_6H_4	9.33 (d, 1H, H_2 of quinoline); 8.83 (d, 1H, H_4 of quinoline); 8.13-6.96 (m, 8H, OH, $H_{3,6,7}$ of quinoline, NC_6H_4); 3.97 (s, 2H, C$\underline{H}_2$ of thiazolidinone); 3.90 (s, 3H, OCH_3); 2.43 (s, 3H, CH_3)
IVl	p-F-C_6H_4	9.23 (d, 1H, H_2 of quinoline); 8.90 (d, 1H, H_4 of quinoline); 8.10-7.10 (m, 8H, OH, $H_{3,6,7}$ of quinoline, NC_6H_4); 4.30 (s, 2H, C$\underline{H}_2$ of thiazolidinone); 2.50 (s, 3H, CH_3)**

* Protons of OH groups are exchangeable by D_2O

** d_6-DMSO: dimethylsulfoxide

Table 7: Physical data of 5-benzoyl-8-hydroxyquinoline-2-(3-substituted-4-oxothiazolidin-2-ylidene) hydrazone compounds **(V a-f)**.

No.	R^1	Yield %	M.P°	M.F/ M.Wt	Microanalysis Calculated / found			
					C %	H %	N %	S %
Va	H	58	235-37	$C_{19}H_{14}N_4O_2S$ 362.41	62.97 62.77	3.89 3.39	15.46 15.40	8.85 9.16
Vb	CH_3	66	177-79	$C_{20}H_{16}N_4O_2S$ 376.43	63.81 63.73	4.28 3.65	14.88 14.90	8.52 8.93
Vc	C_2H_5	65	140-42	$C_{21}H_{18}N_4O_2S$ 399.46*	63.14 63.23	4.54 4.72	14.03 14.17	8.03 8.26
Vd	$CH_2CH=CH_2$	69	197-99	$C_{22}H_{18}N_4O_2S$ 402.47	65.65 65.19	4.51 4.05	13.92 13.82	7.97 8.21
Ve	C_4H_9(n)	67	180-82	$C_{23}H_{22}N_4O_2S$ 418.51	66.01 65.87	5.30 4.89	13.39 13.38	7.66 8.00
Vf	C_6H_{11} (c)	62	250-52	$C_{25}H_{24}N_4O_2S$ 444.55	67.54 67.06	5.44 4.64	12.60 12.54	7.21 7.51

*contain 0.5 molecule of water

Table 8: ^{1}H-NMR data of 5-benzoyl-8-hydroxyquinoline-2-(3-substituted-4-oxothiazolidin-2-ylidene) hydrazone compounds **(V a-f)**.

No	R^1	^{1}H NMR (δ ppm in $CDCl_3$)*
Va	H	9.10 (d, 1H, H_2 of quinoline); 8.10-7.20 (m, 10H, OH, $H_{3,4,6,7}$ of quinoline, C-Ph); 4.00 (s, 2H, $C\underline{H}_2$ of thiazolidinone); 3.70 (s, 1H, NH)**
Vb	CH_3	8.93 (d, 1H, H_2 of quinoline); 8.20-7.20 (m, 10H, OH, $H_{3,4,6,7}$ of quinoline, C-Ph); 3.86 (s, 2H, $C\underline{H}_2$ of thiazolidinone); 2.80 (s, 3H, CH_3)
Vc	C_2H_5	8.93 (d, 1H, H_2 of quinoline); 8.20-7.20 (m, 10H, OH, $H_{3,4,6,7}$ of quinoline, C-Ph); 3.89 (s, 2H, $C\underline{H}_2$ of thiazolidinone); 3.48 (q, 2H, $C\underline{H}_2CH_3$); 0.66 (t, 3H, $CH_2C\underline{H}_3$)
Vd	$CH_2CH=CH_2$	9.00 (d, 1H, H_2 of quinoline); 8.50-7.40 (m, 10H, OH, $H_{3,4,6,7}$ of quinoline, C-Ph); 5.80-5.10 (m, 1H, $C\underline{H}=CH_2$); 4.80 (t, 2H, $CH=C\underline{H}_2$); 4.00 (d, 2H, NCH_2); 3.90 (s, 2H, $C\underline{H}_2$ of thiazolidinone)
Ve	C_4H_9 (n)	8.96 (d, 1H, H_2 of quinoline); 8.50-7.40 (m, 10H, OH, $H_{3,4,6,7}$ of quinoline, C-Ph); 3.80 (s, 2H, $C\underline{H}_2$ of thiazolidinone); 3.33 (t, 2H, NCH_2); 1.50-0.70 (m, 4H, $C\underline{H}_2C\underline{H}_2CH_3$); 0.50 (t, 3H, $CH_2C\underline{H}_3$)
Vf	C_6H_{11} (c)	9.10 (d, 1H, H_2 of quinoline); 8.60-7.46 (m, 10H, OH, $H_{3,4,6,7}$ of quinoline, C-Ph); 4.33-3.80 (m, 1H, $NC\underline{H}$ of cyclohexyl); 3.86 (s, 2H, $C\underline{H}_2$ of thiazolidinone); 1.90-0.50 (m, 10H, $(C\underline{H}_2)_5$ of cyclohexyl)

* Protons of OH groups are exchangeable by D_2O

** d_6-DMSO: dimethylsulfoxide

Method: Agar cup diffusion method.[40, 41]

(i) Preparation of the medium

Cultures were grown on nutrient agar medium of the following composition (g / L): Peptone 5 g, beef extract 3 g, NaCl 3 g, and agar agar 15 g while the tested fungal species were grown on sterilized sabouraud's dextrose agar of the following composition (g / L): Peptone 10 g, glucose 40 g, agar 20 g, and chloramphenicol 0.5 g (as a bacteriostatic agent). Streptomycin 1% solution and Cansten (Clotrimazol 1% solution) were used as positive controls for bacteria and fungi respectively. The media were inoculated at 121° and 1.5 atm. for 20 m, distributed in sterile plates (20 ml per plates) and allowed to solidify. The tested bacteria species were firstly grown in liquid culture for 48 h, and then 1 ml of each bacterial suspension was poured on the solidified agar medium and thoroughly distributed on the agar surface with a sterile L shape glass bar. Cups were made in the solidified agar (6 / plate) with the aid of sterile cork borer, which were filled with 10 ul of the tested compounds. Five of these cups were devoted for the tested compounds, while the last one was left as control for the solvent.

(ii) Preparation of the solution of the tested compounds

The compounds were dissolved in DMSO and were tested at a concentration of 1% (w/v).

(iii) Procedure

An aliquot of 0.1 ml of each of the tested compound solution was pipetted into the appropriate cup; the last cup was used as control test for pure DMSO. The plates were left for one hour at room temperature to allow for prediffusion, then incubated at 37° for 48-96 hours and the inhibition zones around cavities were measured in mm. Results were recorded as the average of three readings in Tables 9-12.

Table 9: Antibacterial activity for 5-acetyl (or 5-benzoyl)-8-hydroxyquinoline-4-substituted thiosemicarbazone compounds **(IIb-m, IIIa-m)** measured by inhibition zone test (mm).

No	R	R^1	*M. luteus*	*S. aureus*	*P. aeroginosa*	*S. marscens*
IIb	CH_3	CH_3	-	-	-	8
IIc	CH_3	C_2H_5	-	-	-	10
IIf	CH_3	C_6H_{11}(c)	-	-	-	7
IIg	CH_3	C_6H_5	-	-	-	7
IIh	CH_3	o-CH_3-C_6H_4	-	-	-	7
Iii	CH_3	m-CH_3-C_6H_4	-	-	-	10
IIj	CH_3	p-CH_3-C_6H_4	-	-	-	13
IIk	CH_3	p-OCH_3-C_6H_4	-	-	-	10
IIl	CH_3	p-F-C_6H_4	-	15	-	8
IIm	CH_3	o-Cl-C_6H_4	-	15	-	10
IIIa	C_6H_5	H	-	20	-	12
IIIb	C_6H_5	CH_3	-	-	-	12
IIIc	C_6H_5	C_2H_5	7	-	-	10
IIIg	C_6H_5	C_6H_5	-	-	-	8
IIIi	C_6H_5	m-CH_3-C_6H_4	-	-	-	8
IIIj	C_6H_5	p-CH_3-C_6H_4	-	-	-	8
IIIk	C_6H_5	p-OCH_3-C_6H_4	-	-	-	8
IIIl	C_6H_5	p-F-C_6H_4	10	-	-	8
IIIm	C_6H_5	o-Cl-C_6H_4	7	-	-	8
Streptomycin			50	50	12	37

Table 10: Antibacterial activity for 5-acetyl (or 5-benzoyl)-8-hydroxy-quinoline-2-(3-substituted-4-oxothiazolidin-2-ylidene)hydrazone compounds **(IVa-j, Va,c,d,f)** measured by inhibition zone test (mm).

No	R	R^1	*M. luteus*	*S. aureus*	*P. aeroginosa*	*S. marscens*
IVa	CH_3	H	-	-	-	12
IVb	CH_3	CH_3	12	15	-	10
IVc	CH_3	C_2H_5	-	-	-	7
IVd	CH_3	$CH_2CH=CH_2$	-	-	-	7
IVe	CH_3	C_4H_9(n)	-	-	-	10
IVf	CH_3	C_6H_{11}(c)	10	10	-	-
IVg	CH_3	C_6H_5	8	-	-	8
IVh	CH_3	o-CH_3-C_6H_4	-	-	-	10
IVi	CH_3	m-CH_3-C_6H_4	-	-	-	8
IVj	CH_3	p-CH_3-C_6H_4	-	-	-	8
Va	C_6H_5	H	20	20	-	-
Vc	C_6H_5	C_2H_5	-	-	-	8
Vd	C_6H_5	$CH_2CH=CH_2$	-	-	-	9
Vf	C_6H_5	C_6H_{11}(c)	10	10	-	8
Streptomycin			50	50	12	37

Table 11: Antifungal activity for 5-acetyl (or 5-benzoyl)-8-hydroxy quinoline-4-substituted thiosemicarbazone compounds **(IIa-m, IIIa,g-j)** measured by inhibition zone test (mm).

No	R	R^1	*C albicans*	*T. rubrum*	*G. candidum*	*S. brevicaulis*
IIa	CH_3	H	12	15	7	-
IIb	CH_3	CH_3	16	25	12	17
IIc	CH_3	C_2H_5	17	20	17	26
IId	CH_3	$CH_2CH=CH_2$	14	13	9	-
IIe	CH_3	C_4H_9(n)	19	26	14	22
IIf	CH_3	C_6H_{11}(c)	-	12	8	9
IIg	CH_3	C_6H_5	11	14	9	9
IIh	CH_3	o-CH_3-C_6H_4	9	15	8	-
Iii	CH_3	m-CH_3-C_6H_4	-	10	-	-
IIj	CH_3	p-CH_3-C_6H_4	10	17	-	-
IIk	CH_3	p-OCH_3-C_6H_4	10	20	-	-
IIl	CH_3	p-F-C_6H_4	12	21	7	6
IIm	CH_3	o-Cl-C_6H_4	11	18	7	-
IIIa	C_6H_5	H	9	13	9	-
IIIg	C_6H_5	C_6H_5	24	30	17	17
IIIh	C_6H_5	o-CH_3-C_6H_4	16	15	12	12
IIIi	C_6H_5	m-CH_3-C_6H_4	16	23	8	15
IIIj	C_6H_5	p-CH_3-C_6H_4	17	25	15	11
Clotrimazol			22	52	18	19

Table 12: Antifungal activity for 5-acetyl (or 5-benzoyl)-8-hydroxy-quinoline-2-(3-substituted-4-oxothiazolidin-2-ylidene)-hydrazone compounds **(IVa,b,f & Va-e)** measured by inhibition zone test (mm).

No	R	R^1	*C albicans*	*T. rubrum*	*G. candidum*	*S. brevicaulis*
IVa	CH_3	H	9	-	-	-
IVb	CH_3	CH_3	16	12	13	13
IVf	CH_3	C_6H_{11}(c)	-	-	7	-
Va	C_6H_5	H	9	-	8	-
Vb	C_6H_5	CH_3	-	-	6	-
Vc	C_6H_5	C_2H_5	-	-	8	-
Vd	C_6H_5	$CH_2CH=CH_2$	7	-	-	-
Ve	C_6H_5	C_4H_9(n)	7	-	7	-
Clotrimazol			22	52	18	19

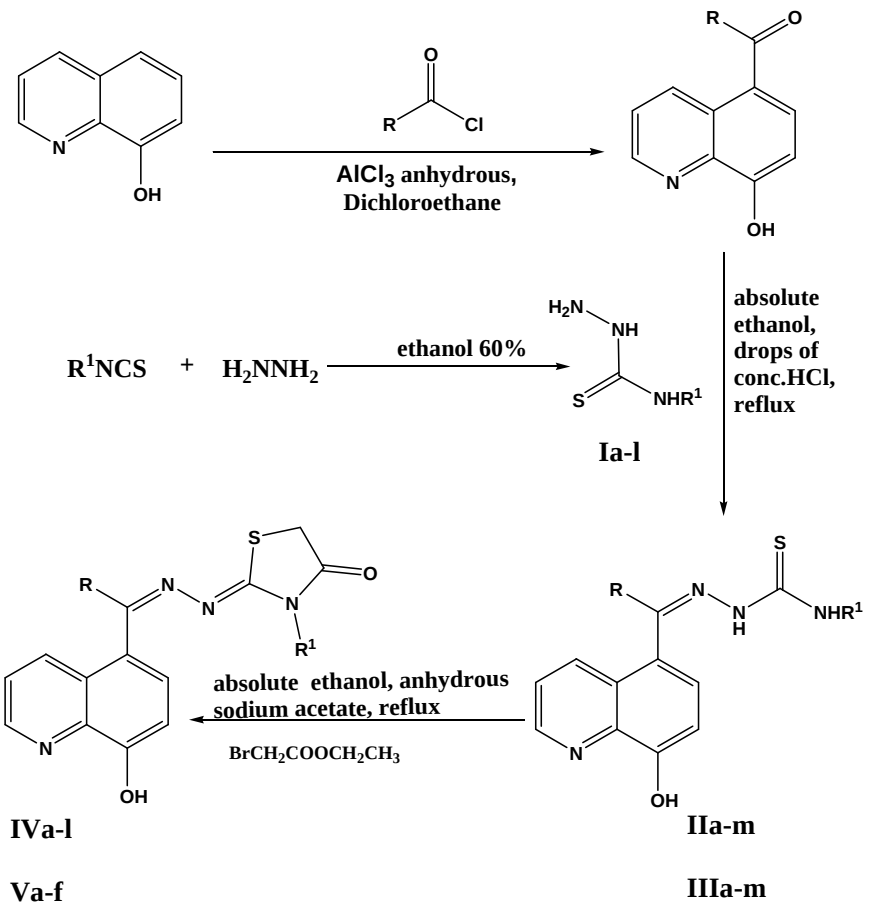
RESULTS AND DISCUSSION

Chemistry

In the present investigation 5-acetyl (or 5-benzoyl)-8-hydroxyquinoline were prepared by the reaction of 8-hydroxyquinoline with acetyl chloride or benzoyl chloride in the presence of anhydrous aluminum chloride as a catalyst using dichloroethane as a solvent under Friedel-Crafts acylation reaction condition.[39] The designed 5-acetyl (or 5-benzoyl)-8-hydroxy- quinoline-4-substituted thiosemi-carbazone compounds **(IIa-m, IIIa-m)** were prepared by the condensation of 5-acetyl (or 5-benzoyl)-8-hydroxy-quinoline with an equimolar amount of thiosemicarbazide or the appropriate 4-substituted-3- thiosemicarbazides **(Ia-l)** in acidified ethanol under reflux for 2-8 hr. The IR spectra of such thiosemicarbazones lacked the band due to the carbonyl function of the starting 5-acetyl (or 5-benzoyl)-8-hydroxy quinoline and showed bands due to NH functions at 3450-3340 cm^{-1} and 3300-3200 cm^{-1}, the mixed vibrational coupling of the NCS moieties at 1540-1520 cm^{-1}, 1335-1320 cm^{-1}, 1180-1150 cm^{-1}, and 950-920 cm^{-1}, as well as a band at 1590-1580 cm^{-1} characteristic for C=N and C=C function. In addition to a characteristic band at 3500-3300 cm^{-1} for the stretching vibration of the OH group of 8-hydroxyquinoline. The ^{1}H-NMR data for 5-acetyl-8-hydroxyquinoline-4-substituted thio-semicarbazones **(IIa-m)** revealed the presence of E/Z geometric isomers although TLC showed that they turned out to be single isomer. According to the ^{1}H-NMR spectra, compounds **(IIa-m)** appeared to be mixtures of unequal proportion of two isomers as predicted from the comparative measurements of the signal corresponding to CH_3 group of 5-acetyl-8-hydroxyquinoline. As a representative example, the mass spectrum of 5-acetyl-8-hydroxyquinoline-4-phenyl thiosemicarbazone (IIg) revealed the molecular ion peak M^+ at m/z =336, 5.7%.

5-Acetyl (or 5-Benzoyl)-8-hydroxy quinoline-2-(3-substituted-4-oxothia-zolidin-2-ylidene) hydrazone compounds **(IVa-l, Va-f)** were prepared by the reaction of 5-acetyl (or 5-benzoyl)-8-hydroxyquinoline-4-substituted thiosemicarbazones **(IIa-l, IIIa-f)** with an equimolor amount of ethyl bromoacetate in the presence of anhydrous sodium acetate and reflux in absolute ethanol. The IR spectra were characterized by some general features such as lack of the characteristic bands due to NH and NCS functions and exhibited the characteristic C=O band of the thiazolidinone ring at 1720-1700 cm^{-1}. In addition a band attributed to C=N stretching function at 1620-1590 cm^{-1}. Moreover, all compounds showed the characteristic band at 3500-3300 cm^{-1} attributed to the OH stretching vibration of the 8-hydroxyquinoline.

The following scheme summarizes the sequences of the reactions involved for the preparation of the designed compounds.



Ia-l

IVa-l

IIa-m

Va-f

IIIa-m

R=CH_3 (IIa-m, IVa-I), C_6H_5 (IIIa-m,Va-f)

R^1= H, CH_3, C_2H_5, $CH_2CH{=}CH_2$, C_4H_9(n), C_6H_{11}(c), C_6H_5, o-CH_3-C_6H_4, m-CH_3-C_6H_4, p-CH_3-C_6H_4, p-OCH_3-C_6H_4, p-F-C_6H_4, o-Cl-C_6H_4

Antimicrobial evaluation

In vitro antimicrobial screening: The prepared compounds as 1% (w/v) solution in DMSO were in vitro evaluated for antibacterial activity against Gram-positive bacteria (*Micrococcus luteus, Staphylococcus aureus*), Gram-negative bacteria (*Pseudomononus aeroginosa, Serratia marscens*) and for antifungal activity against *Candida albicans, Trichophyton rubrum, Geotrichum candidum,*and *Scopulariopsis brivicalis* using agar cup diffusion method.[40,41] The zone of inhibition of the test compounds and the reference Streptomycin 1% (w/v) solution and Clotrimazole 1% (w/v) were measured. As a general feature the 5-acetyl (or 5-benzoyl)-8-hydroxyquinoline-4-substituted thiosemicarbazones (**IIb-m**, **IIIa-m)** (Table 9) showed weak activities against *Serratia marscens* and without significant effect against *Micrococcus luteus, Staphylococcus aureus* and *Pseudomononus aeroginosa* compared to Streptomycin and showed moderate to equal activity against fungi such as *Candida albicans, Trichophyton rubrum, Geotrichum candidum,* and *Scopulariopsis brivicalis* compared to Clotrimazol. As a general feature the 5-acetyl (or 5-benzoyl)-8-hydroxyquinoline-2-(3-substituted-4-oxothiazolidin-2-ylidene)hydrazone compounds (**IVa-j**, **Va,c,d,f)** (Table 10) were found to be displaying weak activities against *Serratia marscens* and without significant effect against *Micrococcus luteus, Staphylococcus aureus* and *Pseudomononus aeroginosa* compared to Streptomycin. On the other hand 5-acetyl-8-hydroxyquinoline-4-substituted thiosemicarbazone compounds (**IIa-m)** were more

effective against fungi than 5-benzoyl-8-hydroxyquinoline-4-substituted thiosemicarbazone compounds (**IIIa-m)** (Table 11). They showed scattered moderate activity against *Candida albicans* and *Geotrichum candidum*. In addition, 5-acetyl (or 5-benzoyl)-8-hydroxyquinoline-4-substituted thiosemicarbazone compounds (**IIa-l**, **IIIa-f)** were more effective against fungi than their corresponding thiazolidinones (compounds **IVa,b,f & Va-e)** (Table 12).

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