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Research Article

Synthesis and Anti-Microbial Activity of 3-Hydrazinyl-7-Ethylquinoxaline-2(1*H*)-Thiol Derivatives

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A B S T R A C T

There are various pharmaceutical applications for quinoxaline derivatives. Benzoheterocycles, 6-methylequinoxalin-2,3-diones, and 3-Hydrazinyle are quinoxaline derivatives. 7-Methoxyquinoxaline-2(1H)-thiol Derivatives TLC, Melting Point, FT-IR, and 1HNMR are used to describe quinoxaline compounds such as SG-IA, SG-IB, SG-IC, SG-ID, SG-IE, and SG-IF. Biological activity data showed that SG-IC and SG-IB were moderately active, whereas SG-IA, SG-ID, SG-IE, and SG-IF had average activity when compared to the standard. The test compounds were discovered to be more sensitive to Gram-positive bacteria such as Staphylococcus aureus and Escherichia coli (Gram-negative bacteria).

Keyword: -Anti-Microbial Activity, Chloramphenicol, Ampicillin

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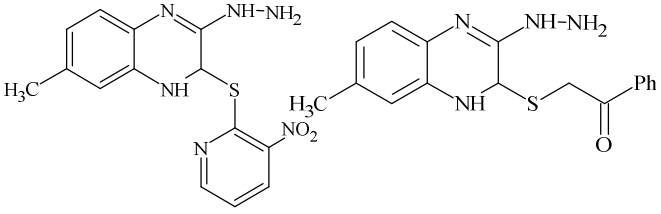
INTRODUCTION:

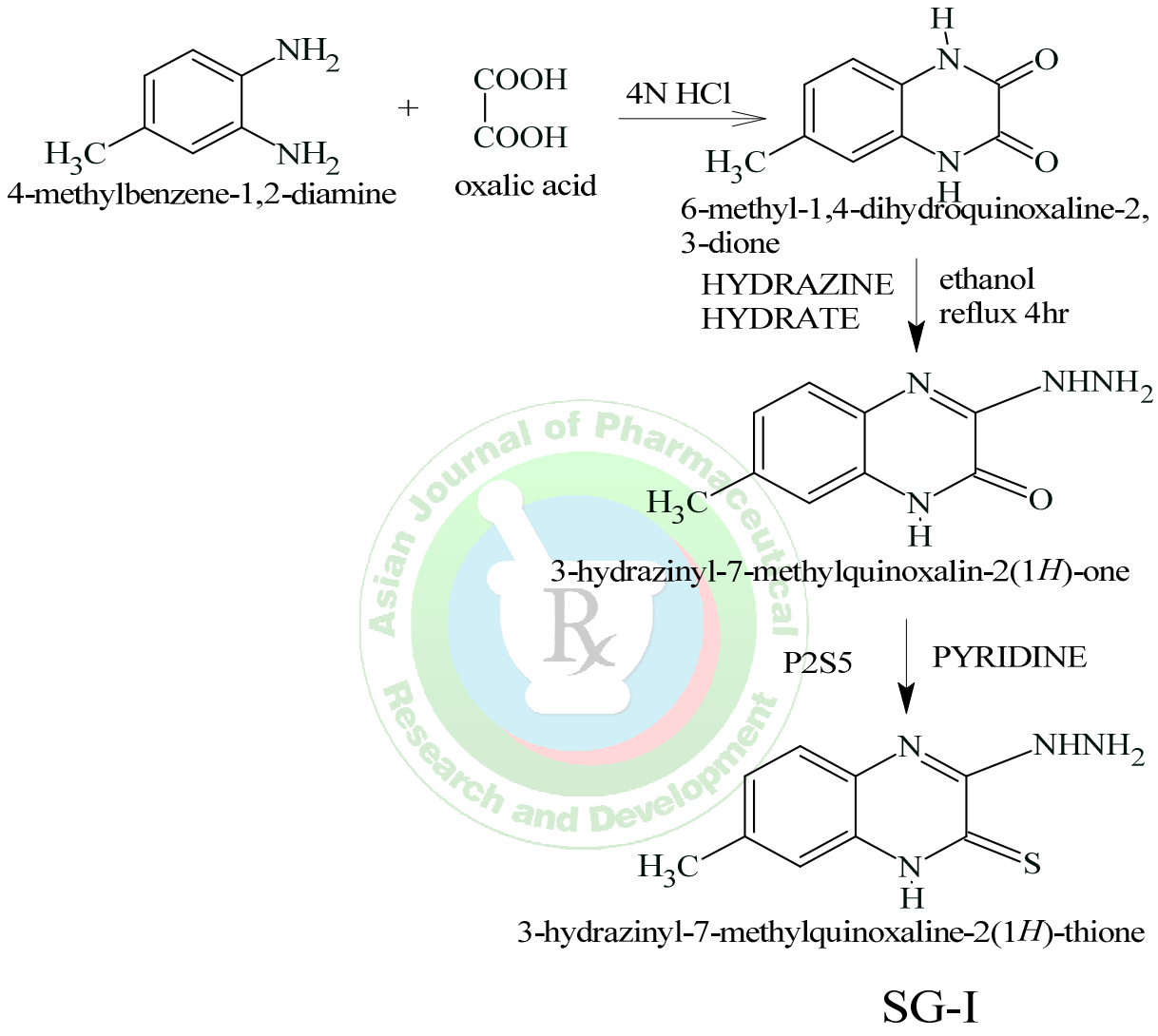
Quinoxaline Compounds containing the nucleus exhibit a broad spectrum of biological activity such as antibacterial, antifungal, antiviral, anticancer, anti-tuberculosis, anti-malarial, and anti-inflammatory properties. Many researchers have reported the synthesis and biological activity of quinoxaline derivatives[1]. Quinoxalines constitute an important class of compounds; some analogs are synthesized and evaluated for antimicrobial activity and many possess diverse biological activities such as insecticidal, fungicidal, herbicidal, and anthelmintic[2].A critical bacterial interaction required for bacteria egress and dissemination involves late-budding domains, which are highly conserved in the matrix protein of many DNA of bacteria. Targeting this interaction, a novel series of 3-hydrazinyl-7-methyl-2-[(3-nitropyridin-2-yl)sulfanyl]-1,2-dihydroquinoxalineand 2-[(3-hydrazinyl-7-methyl-1,2-dihydroquinoxalin-2-yl)sulfanyl]-1-phenylethan-1-oneanalogs were synthesized and evaluated for their ability to inhibit bacterial activity. Among them, compounds demonstrated strong bacterial egress inhibition potential[3].



SG-IA **SG-IC**

1. Presence of a final arylalkyl group substituted at the ortho and para position by a halogen or a methyl group improved potency
2. Substitution of sulfur resulted in greatly reduced activity
3. Methyl substituents on the imido and amide nitrogen atoms resulted in greatly reduced activity and A lipophilic side chain enhances the activity.The presence of a second CH_3 favors antiviral activity
4. No suitable replacement of the methyl substituent on the quinoxaline moiety in the methylene bridge is necessary for the activity

EXPRIMENT



Preparation of 3-hydrazinyl-7-methylquinoxaline-2(1*H*)-thiol Derivatives

A mixture of **3-hydrazinyl-7-methylquinoxaline-2(1*H*)-thiol**[SG-I] (0.01 mol), Substituted halides (0.01 mol) and anhydrous potassium carbonate (2.0 g,0.01mol) in dimethyl Formamide (30 ml) was heated under reflux for 12 h. The solvent was evaporated *in a* vacuum and the obtained residue was washed with water, dried, and recrystallized from ethanol.

Table: -1 Derivatives Of 3-Hydrazinyl-7-Methylquinoxaline-2(1*h*)-Thiolderivatives
[SG-IA to SG-IF]

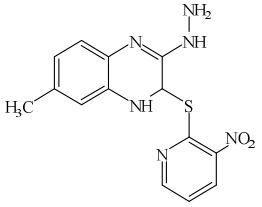
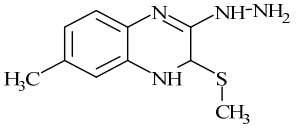
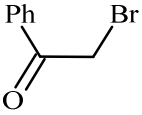
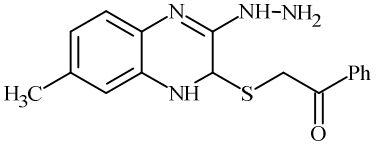
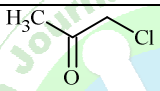
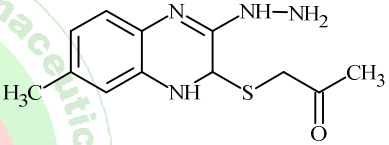
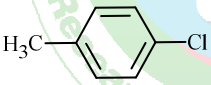
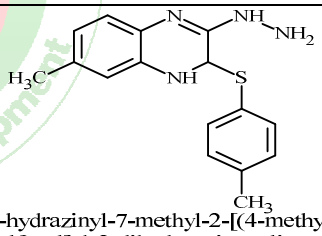
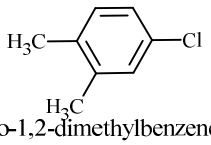
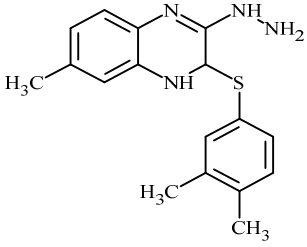
Compound Code	Substituted Halides	Derivatives of 3-hydrazinyl-7-methylquinoxaline-2(1*H*)-thiolDerivatives
SG-IA		 3-hydrazinyl-7-methyl-2-[(3-nitropyridin-2-yl)sulfanyl]-1 ,2-dihydroquinoxaline
SG-IB	CH_3I Methyl iodide	 3-hydrazinyl-7-methyl-2-(methylsulfanyl)-1,2-dihydroquinoxaline
SG-IC	 2-bromo-1-phenylethan-1-one	 2-[(3-hydrazinyl-7-methyl-1,2-dihydroquinoxalin-2-yl) sulfanyl]-1-phenylethan-1-one
SG-ID	 1-chloropropan-2-one	 1-[(3-hydrazinyl-7-methyl-1,2-dihydroquinoxalin-2-yl)sulfanyl]propan-2-one
SG-IE	 1-chloro-4-methylbenzene	 3-hydrazinyl-7-methyl-2-[(4-methylphenyl) sulfanyl]-1,2-dihydroquinoxaline
SG-IF	 4-chloro-1,2-dimethylbenzene	 2-[(3,4-dimethylphenyl)sulfanyl]-3-hydrazinyl-7-methyl -1,2-dihydroquinoxaline

Table: 2 Physicochemical Properties of Derivatives Of Compound 3-Hydrazinylequinoxaline-2(1h)-Thi3-Hydrazinyl-7-Methylquinoxaline-2(1*h*)-Thiolderivatives [SG-IA-IC]

Sr. No	Parameter	SG-IA	SG-IB	SG-IC
1	Molecular Formula	$C_{14}H_{14}N_6O_2S$	$C_{10}H_{14}N_4S$	$C_{17}H_{18}N_4OS$
2	Molecular weight	330.36	222.30	326.41
3	Theoretical yield	3.30gm	2.22gm	3.26gm
4	Practical yield	2.14gm	1.4gm	2.18gm
5	% Yield	64.84%	63.06%	66.87%
6	Melting point	240-245° C	286^0-289° C	305-308° C
7	Recrystallization	Ethanol	Ethanol	Ethanol
8	TLC	Benzene: Chloroform 5:1	Benzene: Chloroform5:1	Benzene: Chloroform5:1
9	R_f Value	0.85	0.96	0.90

Table 3: Physicochemical Properties Of Derivatives Of Compound 3-hydrazinyl-7-methylquinoxaline-2(1*H*)-thiolDERIVATIVES [SG-ID-IF]

Sl. No	Parameter	SG-ID	SG-IE	SG-IF
1	Molecular Formula	$C_{12}H_{16}N_4OS$	$C_{16}H_{18}N_4S$	$C_{17}H_{20}N_4S$
2	Molecular weight	264.34	298.40	312.43
3	Theoretical yield	2.63gm	2.98gm	3.12gm
4	Practical yield	2.14gm	1.4gm	2.18gm
5	% Yield	81.36%	46.97%	69.87%
6	Melting point	240-245° C	286^0-289° C	305-308° C
7	Recrystallization	Ethanol	Ethanol	Ethanol
8	TLC	Benzene: Chloroform 5:1	Benzene: Chloroform5:1	Benzene: Chloroform5:1
9	R_f Value	0.85	0.96	0.90

DATA ANALYSIS

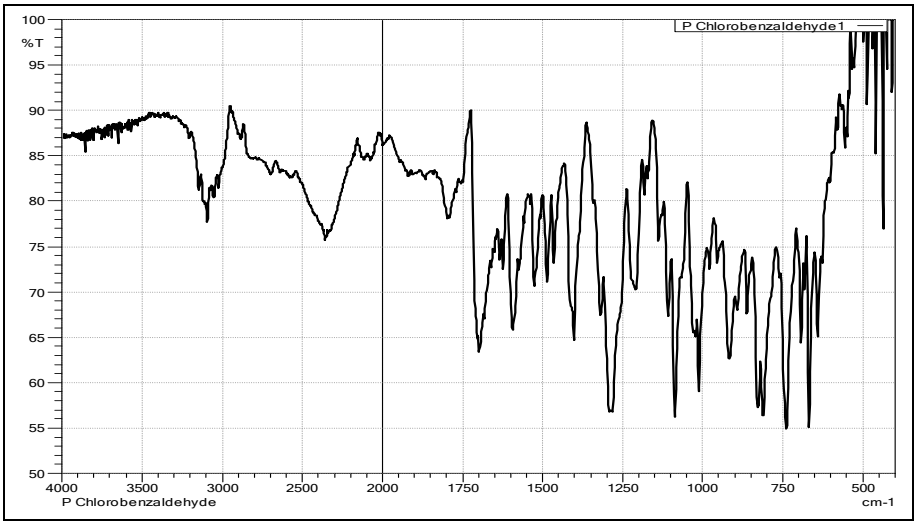


Figure: 1 FT-IR Spectra of 3-hydrazinyl-7-methyl-2-[(3-nitropyridin-2-yl)sulfanyl]-1,2-dihydroquinoxaline [SG-IA]

Table 3: Spectral Data of 3-hydrazinyl-7-methyl-2-[(3-nitropyridin-2-yl) sulfanyl]-1,2-dihydroquinoxaline [SG-IA]

Sr. No	Wave number (cm^{-1})	Functional group assigned
1	3150	N – H Stretch of 2° amine
2	3050	Aromatic C-H Stretch
3	2945	Aliphatic C-H Stretch
4	1618	C = O Stretch
5	1571	C = N Strech
6	1488,1443	C =C Strech
7	954	C-O Strech
8	751	N-H bend

^{1}H NMR (300 MHz, $CDCl_3$) δ : 8.43 (d, *J*= 2.7Hz,1H), 8.06 (dd, *J*=2.4 Hz ,*J'*=9 Hz, 1H) , 7.59 (d ,*J*=9.0 Hz , 1H) , 5.72(br,1H), 3.68(t, *J*= 6.0 Hz, 3H), 3.17 (d, *J*= 4.5 Hz ,2H), 2.75(t, *J*= 6.0 Hz, 2H), 2.48 (s, 6H), 2.027-1.948 (m,2H).^{13} C NMR(300 MHZ,$CDCl_3$) δ 146.50, 145.11, 143.49, 142.14, 136.09, 125.40 ,120.97, 118.41, 58.29, 44.75, 41.12, 28.45, 24.40. HRMS (EI+ Mode) exact mass calculated for $C_{14}H_{20}N_6O_2$ 304.1648, found 304.1653.

Figure: - 2 FT-IR Spectra of 2-[(3-hydrazinyl-7-methyl-1,2-dihydroquinoxalin-2-yl) sulfanyl]-1-phenylethan-1-one [SG-IC]

Table: 4 FT-IR Spectral Data of 2-[(3-hydrazinyl-7-methyl-1,2-dihydroquinoxalin-2-yl) sulfanyl]-1-phenylethan-1-one [SG-IC]

Sr. No	Wave number (cm^{-1})	Functional group assigned
1	3150	N – H Stretch of 2° amine
2	3050	Aromatic C-H Stretch
3	2945	Aliphatic C-H Stretch
4	1618	C = O Stretch
5	1571	C = N Strech
6	1488,1443	C =C Strech
7	954	C-O Strech
8	751	N-H bend

^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.67 (d, *J*= 2.7 Hz ,1H), 8.35(dd, *J*=2.7 Hz ,*J'*=9.3 Hz, 1H) , 7.76 (d ,*J*=9.3 Hz, 1H) , 7.43-7.31 (m,5H), 6.25(br ,1H),4.82 (d ,*J* =5.7 Hz, 2H). ^{13} C NMR(300 MHz, CDCl3) δ 149.09, 145.16, 144.07, 140.25, 137.04, 134.82, 128.93,128.04,126.85,124.33,124.13,45.74. HRMS (EI+ Mode) exact mass calculated for $C_{15}H_{11}ClN_4O_2$ 314.0571, found 314.0571

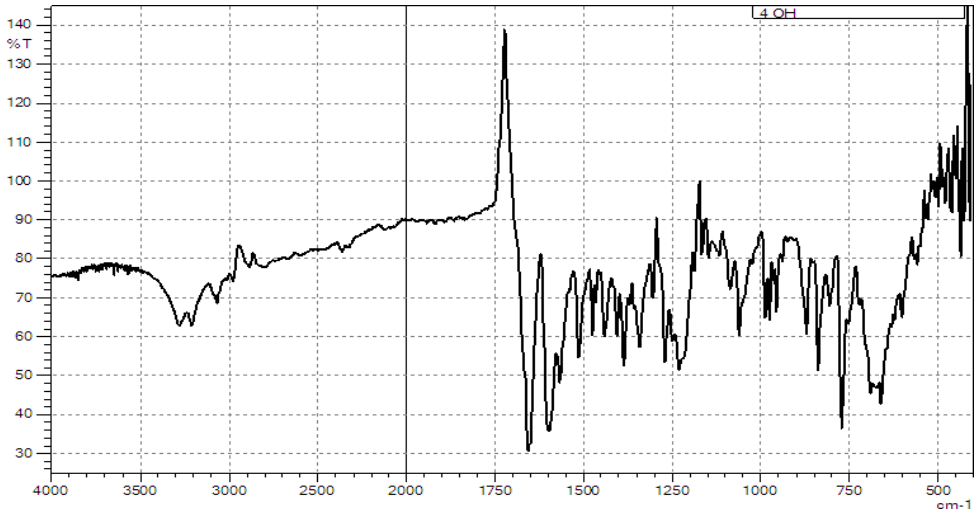


Figure: 3 FT-IR Spectra of 1-[(3-hydrazinyl-7-methyl-1,2-dihydroquinoxalin-2-yl)sulfanyl]propan-2-one [SG-ID]

Table: 5 FT-IR Spectral Data of 1-[(3-hydrazinyl-7-methyl-1,2-dihydroquinoxalin-2-yl)sulfanyl]propan-2-one [SG-ID]

Sr. No	Wave number (cm^{-1})	Functional group assigned
1	3150	N – H Stretch of 2^{o} amine
2	3050	Aromatic C-H Stretch
3	2945	Aliphatic C-H Stretch
4	1618	C = O Stretch
5	1571	C = N Strech
6	1488,1443	C =C Strech
7	954	C-O Strech
8	751	N-H bend

^{1}H NMR (300 MHz, $CDCl_3$) 4b δ : 8.70 (d, *J*= 2.4 Hz ,1H), 8.38(dd, *J*=2.7 Hz ,*J'*=9.3 Hz, 1H) , 7.78 (d ,*J*=9.3 Hz , 1H) , 6.00(br ,1H), 3.22 (d ,*J*=5.1 Hz, 3H). ^{13}C NMR (300 MHZ, DMSO-d_6) δ 150.18, 145.50, 142.73, 140.86, 133.53, 126.29, 124.00,123.58,28.38.HMS (EI+ Mode) exact mass calculated for $C_9H_7ClN_6O_2$ 238.0258, found 238.0235.

BIOLOGICAL ACTIVITY

The cup plate method determined the minimum inhibitory concentration (MIC). Ciprofloxacin was employed during the test procedures as a reference. The MIC of the synthesized compounds ranges between 250-500 µg/ml.

SG-IC, SG-IB, were found moderately active, while SG-IA, SG-IE, SG-ID and SG-IF were found to have an average activity compared with standard. Test compounds were found to be more sensitive toward *Staphylococcus aureus* (Gram-positive bacteria) and *Escherichia coli* (Gram-negative bacteria).

Table: 6 The minimum inhibitory concentration of synthesized compounds [SG-IA to SG-IF] (Against acteria)

Sr No	CompoundCode	*Escherichiacoli (Gram-ve)*			*S. aureus (gram+ve)*		
		Concentration of derivatives (µg/ml)			Concentration of derivatives (µg/ml)		
		250	500	750	250	500	750
		Meanzone of Inhibition (mm)					
1	SG-IA	12	13	13	11	12	15
2	SG -IB	10	11	11	11	11	12
3	SG -IC	15	19	22	13	19	21
4	SG -ID	10	11	11	11	11	12
5	SG -IE	14	22	22	12	16	20
6	SG -IF	18	18	19	12	16	20
7	Ampicillin	25	25	25	25	25	25

Note: -Standard(S) = Ampicillin Control (C) = DMF (Dimethyl Formamide)

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