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Synthesis and biological activity of (Z) –N-(5-Benzylidene-4-Oxo-2-Substituted Phenylthiazolidin-3-yl)-5-((1, 3-dioxoisoindolin-2-YL) methyl)-2-hydroxybenzamide

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ABSTRACT

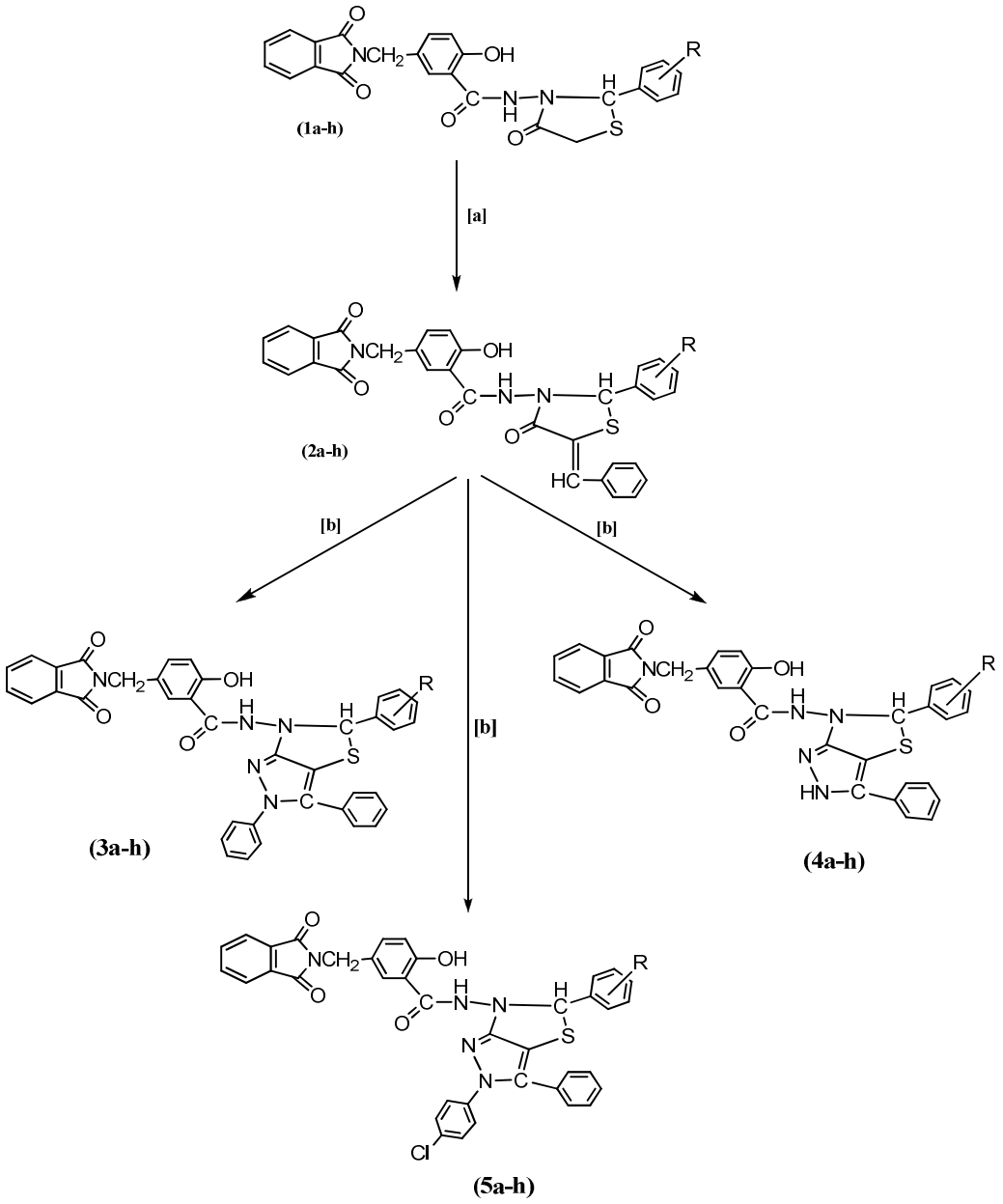
5-((1,3-dioxoisoindolin-2-yl)methyl)-2-hydroxy-N-(4-oxo-2-phenylthiazolidin-3-yl)benzamide ***(1a-h)*** *undergoes facile condensation with aromatic aldehydes in the presence of sodium ethanolate to afford the corresponding N-(5-benzylidene-4-oxo-2-phenylthiazolidin-3-yl)-5-((1,3-dioxoisoindolin-2-yl)methyl)-2-hydroxybenzamide* ***(2a-h)*** *in good yields. These compounds* ***(2a-h)*** *on reaction with hydrazine, phenyl hydrazine and 4-chlorophenylhydrazine in sodium acetate and acetic acid gave appropriate pyrazole derivatives* ***(3a-h), (4a-h) and (5a-h)****. The structures of these compounds were established on the basis of analytical data,* ^{1}*H-NMR,* ^{13}*C-NMR and IR spectral data. All the newly synthesized compounds were evaluated for their antibacterial and antifungal activities. In summary, preliminary results indicate that some of the newly synthesized title compounds exhibited promising antibacterial activities and they warrant more consideration as prospective antimicrobials.*

Keywords: 4-thiozolidinone, 5-benzylidene-2-phenylthiazolidin-4-one, pyrazole, antimicrobial activity.

INTRODUCTION

Bacterial resistance to antibacterial agents or antibiotics is of grave concern in the medical community, as many species of bacteria have evolved resistance to certain antibiotics and synthetic agents. Therefore, there could be a rapidly growing global crisis in the clinical management of life-threatening infectious diseases caused by multi drug resistant strains of the Gram-positive pathogens and Gram-negative. To meet this crisis successfully, many researchers across the globe are working on new compounds which can selectively attack novel targets in microorganisms. Hence, the development of novel, potent, and unique antibacterial agents is the pre eminent way to overcome bacterial resistance and develop effective therapies.

Hydrazide and their heterocyclised products display diverse biological activities including antibacterial, antifungicidal, analgesic, anti-inflammatory properties[1-15].These



SCHEME – 1

(a) (CH_3CH_2ONa, Dioxane) / Benzaldehide, (b) Phenylhydrazine / (Sodium acetate-Acetic acid)

Where, R = (a) C_6H_5 (e) 4-OH-3-OCH_3-C_6H_3

(b) 4-OH-C_6H_4 (f) 4- Cl- C_6H_4

(c) 2-OH-C_6H_4 (g) 2-NO_2-C_6H_4

(d) 4-OCH_3-C_6H_4 (h) 5-Br-2-OH-C_6H_3

heterocyclic systems find wide use in medicine, agriculture and industry. One of the hydrazides, 5-((1,3-dioxoisoindolin-2-yl)methyl-2-hydroxybenzohydrazide and their condensed products play a vital role in medicinal chemistry[16-18]. 4-Thiazolidinones and its arylidene compounds give good pharmacological properties[19-23]. 4-thiazolidinones are also known to exhibit antitubercular[24], antibacterial[25], antifungal[26] and anticonvulsant activities. Hence, it was thought of interest to merge both of thiazolidinone and 5-((1, 3-dioxoisoindolin-2-yl) methyl-2-hydroxybenzohydrazide moieties which may enhance the drug activity of compounds to some extent, or they might possess some of the above mentioned biological activities. From this point of view, the objective of the present work is to prepare new derivatives of 5-((1, 3-dioxoisoindolin-2-yl) methyl)-2-hydroxybenzohydrazide containing thiazolidinone moiety. Hence the present communication comprises the synthesis of 5-((1, 3-dioxoisoindolin-2-yl) methyl)-N-(3, 5-diphenyl-2H-pyrazolo [3, 4-d] thiazol-6(5H)-yl)-2-hydroxybenzamide derivatives. The synthetic approach is shown in scheme-1.

MATERIALS AND METHODS

Melting points were determined in open capillary tubes and were uncorrected. The IR spectra were recorded in KBr pellets on a Nicolet 400D spectrometer and ^{1}H NMR and ^{13}C NMR spectra were recorded in DMSO with TMS as internal standard on a Bruker spectrometer at 400 MHz and 100 MHz, respectively. LC-MS of selected samples taken on LC-MSD-Trap-SL_01046.

Preparation of (Z)-N-(5-benzylidene-4-oxo-2-phenylthiazolidin-3-yl)-5-((1,3-dioxoisoindolin -2-yl)methyl)-2-hydroxybenzamide (2a-h) :-

General procedure:– An equimolar solution of 5-((1,3-dioxoisoindolin-2-yl)methyl)-2-hydroxy-N-(4-oxo-2-phenylthiazolidin-3-yl)benzamide **(1a-h)** and benzaldehyde in dioxane (50 ml) in the presence of C_2H_5ONa were refluxed for about 3 hr. The solvent was removed in vacuum. The resulting product was purified by column chromatography technique and recrystallized from methanol to yield compound **(2a-h).** The yields, melting points and other characterization data of these compounds are given in Table -1.

Preparation of 5-((1,3-dioxoisoindolin-2-yl)methyl)-2-hydroxy-N-(2,3,5-triphenyl-2H-pyrazolo[3,4-d]thiazol-6(5H)-yl)benzamide (3a-h) :-

General procedure:- A mixture (Z)-N-(5-benzylidene-4-oxo-2-phenylthiazolidin-3-yl)-5-((1,3-dioxoisoindolin-2-yl)methyl)-2-hydroxybenzamide **(2a-h)** (0.01 mole) in acetic acid-sodium acetate system (50 ml) and phenyl hydrazine (0.01mole) were refluxed for 6 h. The solvent was then removed to get a residue, which was dissolved in benzene and passed through a column of silica gel using benzene: chloroform (8:2; v/v) mixture as eluent. The eluate was concentrated and the product crystallized from alcohol to give 5-((1,3-dioxoisoindolin-2-yl)methyl)-2-hydroxy-N-(2,3,5-triphenyl-2H-pyrazolo[3,4-d]thiazol-6(5H)-yl)benzamide **(3a-h)**, which were obtained in 52-65% yield. The yields, melting points and other characterization data of these compounds are given in Table -2.

Preparation of 5-((1,3-dioxoisoindolin-2-yl)methyl)-N-(3,5-diphenyl-2H-pyrazolo[3,4-d]thiazol-6(5H)-yl)-2-hydroxybenzamide (4a-h) :-

General procedure:- A mixture (Z)-N-(5-benzylidene-4-oxo-2-phenylthiazolidin-3-yl)-5-((1,3-dioxoisoindolin-2-yl)methyl)-2-hydroxybenzamide **(2a-h)** (0.01 mole) in acetic acid-sodium acetate system (50 ml) and hydrazine (0.01mole) were refluxed for 6 h. The solvent was then removed to get a residue, which was dissolved in benzene and passed through a column of silica gel using benzene: chloroform (8:2; v/v) mixture as eluent. The eluate was concentrated and the product crystallized from alcohol to give 5-((1,3-dioxoisoindolin-2-yl)methyl)-N-(3,5-diphenyl-

2H-pyrazolo[3,4-d]thiazol-6(5H)-yl)-2-hydroxybenzamide **(4a-h)**, which were obtained in 52-65% yield. The yields, melting points and other characterization data of these compounds are given in Table -3.

Preparation of N-(2-(4-chlorophenyl)-3,5-diphenyl-2H-pyrazolo[3,4-d]thiazol-6(5H)-yl)-5-((1,3-dioxoisoindolin-2-yl)methyl)-2-hydroxybenzamide (5a-h) :-

General procedure:- A mixture (Z)-N-(5-benzylidene-4-oxo-2-phenylthiazolidin-3-yl)-5-((1,3-dioxoisoindolin-2-yl)methyl)-2-hydroxybenzamide **(2a-h)** (0.01 mole) in acetic acid-sodium acetate system (50 ml) and 4-chlorophenyl hydrazine (0.01mole) were refluxed for 6 h. The solvent was then removed to get a residue, which was dissolved in benzene and passed through a column of silica gel using benzene: chloroform (8:2 ; v/v) mixture as eluent. The eluate was concentrated and the product crystallized from alcohol to give N-(2-(4-chlorophenyl)-3,5-diphenyl-2H-pyrazolo[3,4-d]thiazol-6(5H)-yl)-5-((1,3-dioxoisoindolin-2-yl)methyl)-2-hydroxybenzamide **(5a-h)**, which were obtained in 52-65% yield. The yields, melting points and other characterization data of these compounds are given in Table -4.

RESULTS AND DISCUSSION

It was observed that 5-((1,3-dioxoisoindolin-2-yl)methyl)-2-hydroxy-N-(4-oxo-2-phenylthiazolidin-3-yl)benzamide **(1a-h)**, on condensation with benzaldehide, yields (Z)-N-(5-benzylidene-4-oxo-2-phenylthiazolidin-3-yl)-5-((1,3-dioxoisoindolin-2-yl)methyl)-2-hydroxy benzamide **(2a-h)**. The structures of **(2a-h)** were confirmed by IR spectra showing an absorption band at 3030-3080 cm^{-1} (C-H, of Ar.), 3450-3550 cm^{-1} (-OH), 2810-2852 cm^{-1} (-OCH_3), 3285, 1345 (-NH-), 1685(>C=O, amide), 1738 (>C=O,),1868 (>C=CH-). ^{1}H NMR: 8.53 (s, 1H, -CONH-), 4.15 (s, 1H, -N-CH-),6.86(>C=CH). 6.90 – 7.95 (9H, m) (Ar - H), 5.30-5.50 (1H, s) (-OH), 3.90 (3H, s) (-OCH3),4.68(-CH_2-,thiazolidinone). ^{13}C NMR (400 MHz, DMSO -d_6), δ ppm : 164.5 (>C=O, thiazolidinone), 170(>C=O, amide),74.60(-N-CH-),132.5,128.4(>C=CH-), 68 (-CH_2-,thiazolidinone).. The C, H, N analysis data, chemical formula ,M.P. and yield of all compounds are presented in Table -1.

The structures assigned to 5-((1,3-dioxoisoindolin-2-yl)methyl)-2-hydroxy-N-(2,3,5-triphenyl-2H-pyrazolo[3,4-d]thiazol-6(5H)-yl)benzamide **(3a-h)**, were supported by the IR spectra showing an absorption bands at 718cm^{-1} (C-S-C of thiazolidinone ring), 3030-3080 cm^{-1} (C-H, of Ar.), 3450-3550 cm^{-1} (-OH), 1660-1670 cm^{-1} (-CONH), the band at 1738 for (>C=O, thiazolidinone) was disappear and new band at 1476 for (-NH-N<) conform the formation of **(3a-h)** compound. ^{1}H NMR: 6.90-7.95 (14H, m) (Ar-H), 3.85-3.95 (2H, s,-CH_2 of the ring), 5.950-5.959 (1H, s,-CH), 8.20-8.22 (1H, s) (-CONH), 5.33-5.45 (1H, s,-OH), 4.80 (2H, s,CH_2), 3.92 (3H, s,-OCH3). The C, H, N, S analysis data chemical formula, M.P. and yield of all compounds are presented in Table-2.

The structures assigned to 5-((1,3-dioxoisoindolin-2-yl)methyl)-N-(3,5-diphenyl-2H-pyrazolo[3,4-d]thiazol-6(5H)-yl)-2-hydroxybenzamide **(4a-h)**, were supported by the IR spectra showing an absorption bands at 724cm^{-1} (C-S-C of thiazolidinone ring), 3028-3074 cm^{-1} (C-H, of Ar.), 3446-3548 cm^{-1} (-OH), 1657-16768 cm^{-1} (-CONH), the band at 1738 for (>C=O, thiazolidinone) was disappear and new band at 1486 for (-NH-N<) conform the formation of **(4a-h)** compound. ^{1}H NMR: 6.87-7.90 (9H, m, Ar-H), 3.84-3.92 (2H, s,-CH_2 of the ring), 5.95-5.95 (1H, s,-CH), 8.22-8.26 (1H, s,-CONH), 5.33-5.45 (1H, s,-OH), 3.90 (3H, s,-OCH3). The C, H, N, S analysis data chemical formula, M.P. and yield of all compounds are presented in Table-3.

Table: 1 Analytical data and elemental analysis of compounds (2a-h)

Compd.	Molecular formula (Mol.wt.)	Yield	M.P. ^{0}C	Elemental Analysis							
				%C		% H		%N		%S	
				Found	Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.
2a	$C_{26}H_{18}N_3O_5S$ (462)	70	214-218	64.92	64.93	5.17	5.19	9.07	9.09	13.84	13.85
2b	$C_{26}H_{18}N_3O_4S$ (492)	64	220-221	63.43	63.41	5.29	5.30	8.52	8.54	13.02	13.00
2c	$C_{26}H_{18}N_3O_4S$ (478)	63	200-202	62.75	62.76	5.03	5.04	8.77	8.79	13.39	13.38
2d	$C_{27}H_{20}N_3O_4S$ (478)	55	206-208	62.75	62.76	5.03	5.05	8.76	8.79	13.39	13.38
2e	$C_{27}H_{20}N_3O_5S$ (476)	50	195-198	65.53	65.55	5.06	5.08	8.80	8.82	13.45	13.44
2f	$C_{26}H_{17}N_3O_5SCl$ (506)	59	207-210	61.67	61.66	5.16	5.18	8.33	8.30	12.67	12.64
2g	$C_{26}H_{17}N_4O_5S$ (508)	58	193-195	61.40	61.42	5.13	5.15	8.28	8.26	12.56	12.59
2h	$C_{26}H_{17}N_3O_4SBr$ (489)	55	215-217	63.83	63.80	5.53	5.54	8.58	8.59	13.05	13.08

Table:-2 Analytical Data and Elemental Analysis of Compounds (3a-h)

Compd.	Molecular formula (Mol.wt.)	Yield	M.P. ^{0}C	Elemental Analysis							
				%C		%H		%N		%S	
				Found	Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.
3a	$C_{26}H_{20}N_5O_4S$ (478)	55	265	64.23	64.21	5.67	5.68	14.03	14.05	10.74	10.70
3b	$C_{26}H_{20}N_5O_3S$ (524)	61	262	62.03	62.00	5.74	5.77	12.74	12.76	9.75	9.72
3c	$C_{26}H_{20}N_5O_3S$ (498)	54	259	60.94	60.96	5.35	5.39	13.32	13.33	10.14	10.16
3d	$C_{27}H_{22}N_5O_3S$ (512)	64	260	60.94	60.96	5.35	5.39	13.32	13.33	10.17	10.16
3e	$C_{27}H_{22}N_5O_4S$ (496)	65	264	65.22	65.18	5.41	5.43	13.39	13.42	10.21	10.22
3f	$C_{26}H_{19}N_5O_4SCl$ (534)	58	263	59.45	59.47	5.52	5.54	12.23	12.25	9.34	9.33
3g	$C_{26}H_{19}N_6O_4S$ (554)	52	261	59.15	59.13	5.48	5.51	12.14	12.17	9.26	9.27
3h	$C_{26}H_{19}N_5O_3SBr$ (549)	60	258	66.25	66.26	6.11	6.13	12.89	12.88	9.80	9.81

Table:-3 Analytical Data and Elemental Analysis of Compounds (4a-h)

Compd.	Molecular formula (Mol.wt.)	Yield	M.P. ^{0}C	Elemental Analysis							
				%C		% H		%N		%S	
				Found	Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.
4a	$C_{32}H_{26}N_5O_4S$ (552)	65	210-212	56.74	56.75	5.33	5.35	11.20	11.23	17.15	17.11
4b	$C_{32}H_{26}N_5O_3S$ (602)	60	206-208	54.42	54.44	5.44	5.45	10.42	10.40	15.83	15.84
4c	$C_{32}H_{26}N_5O_3S$ (672)	57	155-158	57.40	57.38	5.13	5.12	10.77	10.76	16.43	16.41
4d	$C_{33}H_{28}N_5O_3S$ (588)	66	130-134	58.40	58.38	5.13	5.12	10.77	10.76	16.43	16.41
4e	$C_{33}H_{28}N_5O_4S$ (570)	62	167-170	46.53	46.54	4.76	4.78	10.03	10.05	15.33	15.31
4f	$C_{32}H_{25}N_5O_4SCl$ (605)	55	181-183	62.78	62.76	5.67	5.68	10.84	10.82	16.51	16.49
4g	$C_{32}H_{25}N_6O_4S$ (636)	49	154-156	58.29	58.28	5.22	5.24	10.03	10.00	15.22	15.24
4h	$C_{32}H_{26}N_5O_3SBr$ (628)	61	190-194	63.84	63.85	5.71	5.73	10.45	10.47	15.97	15.96

Table:-4 Analytical Data and Elemental Analysis of Compounds (5a-h).

Compd.	Molecular formula (Mol.wt.)	Yield	M.P. ^{0}C	Elemental Analysis							
				%C		% H		%N		%S	
				Found	Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.
5a	$C_{32}H_{25}N_5O_4SCl$ (588.5)	58	235	57.74	57.75	5.33	5.35	17.15	17.11	10.77	10.76
5b	$C_{32}H_{25}N_5O_3SCl$ (636.5)	64	342	56.42	56.44	5.44	5.45	15.83	15.84	10.77	10.76
5c	$C_{32}H_{25}N_5O_3SCl$ (708.5)	72	283	55.40	55.38	5.13	5.12	16.43	16.41	10.03	10.05
5d	$C_{33}H_{27}N_5O_3SCl$ (623.5)	62	246	55.40	55.38	5.13	5.12	16.43	16.41	10.84	10.82
5e	$C_{33}H_{27}N_5O_4SCl$ (606.5)	58	284	54.53	54.54	4.76	4.78	15.33	15.31	10.03	10.00
5f	$C_{32}H_{24}N_5O_4SCl_2$ (640)	48	312	58.78	58.76	5.67	5.68	16.51	16.49	10.45	10.47
5g	$C_{32}H_{24}N_6O_4SCl$ (671.5)	60	294	54.29	54.28	5.22	5.24	15.22	15.24	10.23	10.25
5h	$C_{32}H_{25}N_5O_3SClBr$ (643.5)	58	248	59.84	59.85	5.71	5.73	15.97	15.96	10.86	10.87

The structures assigned to N-(2-(4-chlorophenyl)-3,5-diphenyl-2H-pyrazolo[3,4-d]thiazol-6(5H)-yl)-5-((1,3-dioxoisoindolin-2-yl)methyl)-2-hydroxybenzamide **(5a-h)**, were supported by the IR spectra showing an absorption bands at 730 cm^{-1} (C-S-C of thiazolidinone ring), 3032-3078 cm^{-1} (C-H, of Ar.), 3456-3556 cm^{-1} (-OH), 1664-1676 cm^{-1} (-CONH), the band at 1742 for (>C=O, thiazolidinone) was disappear and new band at 1484 for (-NH-N<) conform the formation of **(5a-h)** compound. ^{1}H NMR: 6.87-7.90 (13H, m, Ar-H), 3.83-3.90 (2H, s,-CH_2 of the ring), 5.94-5.98 (1H, s,-CH), 8.24-8.28 (1H, s,-CONH), 5.43-5.52 (1H, s,-OH), 3.85 (3H, s,-OCH3). The C, H, N, S analysis data chemical formula, M.P. and yield of all compounds are presented in Table-4.

The examination of elemental analytical data reveals that the elemental contents are consistence with the predicted structure shown in Scheme-1. The IR data also directs for the assignment of the predicted structure.

Biological Screening

Antibacterial activities

The antibacterial activities of all the compounds **(2a-h),(3a-h), (4a-h) and (5a-h**) were studied against gram-positive bacteria (*Staphylococcus aureus and Bacillus subtilis*) and gram-negative bacteria (*E.coli, and klebsiellapromioe*) at a concentration of 50µg/ML by agar cup plate method. A methanol system was used as control in this method. Similar conditions using tetracycline as a control was used standard for comparison. The area of inhibition of zone measured in cm. Compounds **4d, 4f, 4h, 5d, 5f,** and **5h** were found more toxic for microbes. Other compounds found to be less or moderate active than tetracycline Tables 5, 7, 9 and 11.

Antifungal Activities

The fungicidal activity of all the compounds **(2a-h),(3a-h), (4a-h) and (5a-h**) were studied at 1000 ppm concentration in vitro. Plant pathogenic organisms used were *NigrosporaSp, Aspergillusniger, Botrydepladiathiobromine, and Rhizopusnigricum***,** *Fusariumoxyporium*. The antifungal activity of all the compounds **(2a-h),(3a-h), (4a-h) and (5a-h**) were measured on each of these plant pathogenic strains on a potato dextrose agar (PDA) medium. Such a PDA medium contained potato 200g, dextrose 20g, agar 20g and water 1c. Five days old cultures were employed. The compounds to be tested were suspended (1000ppm) in a PDA medium and autoclaved at 120^o C for 15 min. at 15atm. pressure. These media were poured into sterile Petri plates and the organisms were inoculated after cooling the Petri plates. The percentage inhibition for fungi was calculated after five days using the formula given below:

$$\textbf{Percentage of inhibition} = 100(X-Y) / X$$

Where, X = Area of colony in control plate

Y = Area of colony in test plate.

The fungicidal activity displayed by various compounds **(2a-h),(3a-h), (4a-h) and (5a-h**) are shown in Tables- 6, 8, 10 and 12.

Table:-5 Antibacterial Activity of Compounds (2a-h).

Compounds	Gram +Ve		Gram -Ve	
	Staphylococcus aureus	Bacillus subtilis	E.coli	Klebsiellapromioe
2a	51	53	78	68
2b	60	65	65	55
2c	70	62	51	61
2d	57	56	70	60
2e	65	71	58	68
2f	54	67	71	61
2g	59	68	59	69
2h	61	64	65	55
Tetracycline	62	78	71	81

Table:-6 Antifungal Activity of Compounds (2a-h).

Zone of Inhibition at 1000 ppm (%)					
Compounds	**Nigrospora Sp.**	**Aspergillus Niger**	**Botrydepladia Thiobromine**	**Rhizopus Nigricum**	**Fusarium oxyporium**
2a	67	68	61	72	71
2b	60	72	59	63	58
2c	59	75	73	59	60
2d	69	63	65	61	61
2e	63	69	71	60	63
2f	70	68	68	70	58
2g	64	72	64	63	62
2h	68	64	69	62	68

Table:-7 Antibacterial Activity of Compounds (3a-h)

Compounds	**Gram +Ve**		**Gram -Ve**	
	Staphylococcus aureus	**Bacillus subtilis**	**E.coli**	**Klebsiellapromioe**
3a	54	56	62	56
3b	70	68	69	68
3c	67	61	64	60
3d	64	69	71	68
3e	57	54	63	61
3f	68	70	71	69
3g	63	61	60	62
3h	61	69	56	55
Tetracycline	62	78	71	81

Table:-8 Antifungal Activity of Compounds (3a-h).

Zone of Inhibition at 1000 ppm (%)					
Compounds	**Nigrospora Sp.**	**Aspergillus Niger**	**Botrydepladia Thiobromine**	**Rhizopus Nigricum**	**Fusarium oxyporium**
3a	72	71	61	67	72
3b	63	58	59	60	63
3c	59	60	73	59	59
3d	61	61	65	69	61
3e	60	63	71	63	60
3f	70	58	68	70	70
3g	63	62	64	64	63
3h	62	68	69	68	62

Table:-9 Antibacterial Activity of Compounds (4a-h).

Compounds	Gram +Ve		Gram -Ve	
	Staphylococcus aureus	Bacillus subtilis	E.coli	Klebsiellapromioe
4a	58	61	64	58
4b	70	68	69	68
4c	67	61	64	60
4d	64	69	71	68
4e	57	54	63	61
4f	72	74	80	76
4g	63	61	60	62
4h	65	72	69	78
Tetracycline	62	78	71	81

Table:-10 Antifungal Activity of Compounds (4a-h).

Zone of Inhibition at 1000 ppm (%)					
Compounds	**Nigrospora Sp.**	**Aspergillus Niger**	**Botrydepladia Thiobromine**	**Rhizopus Nigricum**	**Fusarium oxyporium**
4a	72	71	61	67	72
4b	63	58	59	60	63
4c	59	60	73	59	59
4d	61	61	65	69	61
4e	60	63	71	63	60
4f	70	58	68	70	70
4g	63	62	64	64	63
4h	62	68	69	68	62

Table: 11 Antibacterial Activity of Compounds (5a-h).

Compounds	Gram +Ve		Gram -Ve	
	Staphylococcus aureus	Bacillus subtilis	E.coli	Klebsiellapromioe
5a	56	58	62	56
5b	64	69	69	68
5c	68	63	64	60
5d	73	70	71	80
5e	59	56	63	61
5f	71	75	74	82
5g	67	67	60	62
5h	70	68	56	55
Tetracycline	62	78	71	81

Table:-12 Antifungal Activity of Compounds (5a-h).

Zone of Inhibition at 1000 ppm (%)					
Compounds	**Nigrospora Sp.**	**Aspergillus Niger**	**Botrydepladia Thiobromine**	**Rhizopus Nigricum**	**Fusarium oxyporium**
5a	78	74	63	69	66
5b	66	60	61	67	62
5c	62	62	75	62	58
5d	65	66	68	72	63
5e	64	68	74	69	67
5f	72	76	78	82	79
5g	66	66	68	67	66
5h	80	78	72	72	67

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REFERENCES

[1] MR Shiradkar; KK Murahari; HR Gangadasu; T Suresh; CC Kalyan; D Panchal; R Kaur; P Burange;
J Ghogare; V Mokale; M Raut. *Bioorg.Med. Chem.***2007**, 15, 3997.
[2] Y Janin. *Bioorg. Med. Chem.***2007**, 15, 2479.
[3] E Gursoy; N Guzeldemirci-Ulusoy. *Eur. J. Med. Chem.***2007**, 42, 320.
[4] MR Rao; K Hart; N Devanna and KB Chandrasekhar. *Asian J. Chem.***2008**, 20**,**1402.
[5] KB Kaymakcıoglu; EE Oruc; S Unsalan; F Kandemirli; N; Shvets; S Rollas; D Anatholy; *Eur. J. Med. Chem.* **2006**, 41, 1253.
[6] R Kalsi; M. Shrimali; TN Bhalla; JP Barthwal; *Indian J. Pharm. Sci.***2006**, 41,353.
[7] S Gemma; G Kukreja; C Fattorusso; M Persico; M Romano; M Altarelli; L Savini; G Campiani; E Fattorusso; N Basilico. *Bioorg. Med. Chem. Lett.* **2006**, 16, 5384.
[8] D Sriram; P Yogeeswari; K Madhu. *Bioorg. Med. Chem. Lett.***2006**, 15, 4502.
[9] A Nayyar; R Jain. *Curr. Med. Chem.* **2006**, 12, 1873.
[10] RM Fikry; NA Ismael; AA El-Bahnasawy; AA Sayed El-Ahl. *Phosphorus, Sulfur and Silicon.***2006**, 179, 1227.
[11] A Walcourt; M Loyevsky; DB Lovejoy; VR Gordeuk; DR Richardson. *Int. J. Biochem. Cell Biol.***2004**, 36**,** 401.
[12] MG Mamolo; V Falagiani; D Zampieri; L Vio; E Banfi; G Scialino. *Farmaco***2003**, *58,* 631.
[13] N Terzioglu; A Gursoy; *Eur. J. Med. Chem.***2003**, 38, 781.
[14] SG Kucukguzel; EE Oruc; S Rollas; F Sahin; A Ozbek. *Eur. J. Med.Chem.* **2002**, 37, 197.
[15] S Rollas; N Gulerman; H Erdeniz. *Farmaco*, **2002**, 57, 171.
[16] LQ Al- Mawsawi; R Dayam; L Taheri; M Witvrouw; Z Debyser; N Neamati; *Bioorg. Med. Chem. Lett.***2007**, 17(23) 6472.
[17] C Plasencia; R Daym; Q Wang; J Pinski; TR Jr. Burke; DI Quinn; and N Neamati. *Mol. Cancer Ther.* **2005,** 4(7) 1105.
[18] H Zhao; N Neamati; S Sunder; H Hong; S Wang; GW Milne; Y Pommier;TR Jr. Burke. *J. Med. Chem.***1997**, 40(6) 937.
[19] KC Asati; SK srivastava and SD Srivastava. *Ind.J.Chem.*, **2006**,45 (B), 526

[20] A Bishnoi; K Srivastava and CKM Tripathi. *Ind.J.Chem.*, **2006**,45(B)**,** 2136.
[21] NP Shetgiri and AD Chitre. *Ind .J .Chem.* **2006,**45(B), 1308.
[22] R Jadav; S Srivastava and SD Srivastava.*An Indian Journal chem* **2003**,1**,** 95
[23] KK Sivakumar; A Rajasekaran; I Ponnilavarasan; A Somasundaram; R Sivasakthi; S. Kamalaveni. *DerPharmacia Lettre*; **2010**, 2(1):211-219.
[24] KM Mistry and KR Desai. *E- Journal of Chem*.**2004**,1(4), 189.
[25] HS Patel, HJ Mistry. *Phosphorous, Sulfur and Silicon* **2004**,179, 1085.
[26] JJ Bhatt; BR Shah and NC Desai. *Ind .J. Chem.* **1994,** 33B, 189.
[27] N Kumar; JS Jain; R Sinha; VK Garg; SK Bansal. *Der Pharmacia Lettre*; **2009**, 1(1):169-176.
[28] S Srivastava; A Jain and S Srivastava. *J. Indian Chem.Soc.*,**2006**,83, 1118.