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Synthesis and Antimicrobial Activity of New Schiff Base Containing Thiazolidin -4-One and their Spectral Characterization

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Abstract: *Heterocyclic Compounds having a valuable place in a Heterocyclic Chemistry and Heterocyclic Compounds having a excellent properties such as drugs, dyes etc, This compounds are showing anti microbial, anti fungal, anti bacterial, anti inflammatory,anti diabetic, anti hypertensive etc. properties. In present investigation, we have prepared 2-{4-[2-{3,5bis-(4-methoxyphenyl)-4,5-dihydro-pyrazol-1-yl}-2-oxoethoxy] phenyl}-3-(substi tutedphenyl)-1,3-thiazolidin-4-one form N-[{4-[2-{3,5-bis(4-methoxyphenyl)-4,5-dihydro-pyrazol-1-yl}-2-oxoethoxy]phenyl}methylene] substituted aniline and thioglycolic acid. Compound having a excellent properties regarding as per as anti cancer and HIV as compare to this compound. Physical properties of pure crystallized Substance 2-{4-[2-{3, 5-bis (4 – methoxyphenyl) -4, 5- dihydro – pyrazol – 1 – yl } – 2 -oxoethoxy]phenyl -3-(substitutedphenyl) -1,3-thiazolidin-4-one substituted aniline like M.P elementary analysis and spectral data of compound and such as IR and NMR will be evaluated and confirm the structure of compound. All the synthesized products were evaluated for their antimicrobial activity. All the compounds were tested for their antibacterial and antifungal activities by broth dilution method.*

Keywords: *Schiff's base, Thiazolidinones and Antibacterial activity.*

1. INTRODUCTION

Thiazolidines are a class of heterocyclic organic compounds having a 5 membered saturated ring with a thio ether group at 1 position and an amine group in the 3 position. It is sulfur analogue of oxazolidine. Thiazolidines may be synthesized by a condensation reaction between a thiol and an aldehyde or ketone. It is a reversible reaction 4-Thiazolidinone derivatives are an important group of heterocyclic compounds possessing a variety of biological effects[1], including antitumor[2-4], anti-inflammatory[5], antimicrobial [6], antiviral [7], anticonvulsant [8], antifungal [9], antibacterial [10] activities and so on. Some of these analogues have been shown to display a very interesting spectrum of antiviral and anticancer activities[11]. The purine nucleosides have established their importance in curbing human immunodeficiency virus (HIV) infection, by interfering in different steps of HIV life cycle (reverse transcriptase and protease inhibitors). Thiazolidin-4-one a saturated form of thiazole with carbonyl group on fourth carbon has been considered as a magic moiety (wonder nucleus) which posses almost all types of biological activities such as anti-HIV [12-14], anti-diarrheal[15], ,anti histaminic [16], Ca2+ channel blocker [17], cardio protective[18],anti-ischemic[19],anti-platelet activating factor[20], non-peptide thrombin receptor antagonist[21] and tumor necrosis factor-α antagonist activities[22]. Looking at the importance of these heterocyclic nuclei, it is thought of interest to accommodate thiazolidin-4-one and 2- amino benzothiazole moieties in single molecular framework and screen them for their various biological activities. In continuation to our research work on benzo thiazole derivatives. [23, 24]

2. EXPERIMENTAL

Melting points were taken in open capillary tube and were uncorrected. IR spectra were recorded on I.R. Spectrophotometer of Buck scientific Model No. 500 and instrument used for NMR Spectroscopy was Bruker Advance II 400 and DMSO used as internal standard. Solvent used were $CDCl_3$ and DMSO. Purity of the compounds were checked by TLC on silica- G plates. All the compounds were tested for their antibacterial and antifungal activities by broth dilution method

3. MATERIALS AND METHODS

3.1. Preparation of *N*-[{4-[2-(3,5 Bis(4-Methoxyphenyl)-4,5-Dihydro-Pyrazol-1-Yl)-2-Oxo Ethoxy]Phenyl}Methylene] Substituted Aniline (1a-J)

A mixture of 2-(4-{[(2-chlorophenyl)imino]methyl}phenoxy) acetohydrazide (0.1M), ethanol (25ml) and 3-(4-chlorophenyl)-1-(4-methoxyphenyl)prop-2-en-1-one (0.1M) with piperidine (1ml) was refluxed for 16 hours. The resulting mixture was concentrated, cooled and poured into cold water containing 6 to 8 drops of HCl, when orange coloured product separated. It was filtered, washed with water and crystallized from methanol-petroleum ether mixture.

IR;1-c(cm^{-1})**:** 3015(=CH-), 2935 (-CH-stretch), 1720 (>C=Ostretch),1655 (C=N-), 1590 (>C=C<aromatic), 1440 (-CH_2-bend), 1385(-CH_3- bend), 1250 (C-N) 1215 (-N-N-), 1110(-C-O-C).

^{1}H NMR (DMSO); 1-i : 2.5425, doublet (2H) (CH_2 -cyclic), 3.7814, singlet (6H) (-OCH_3-), 4.6601, singlet (2H) (-CH_2-),5.0071 triplet (1H) (-CH<) 8.5118, singlet (1H) (Ar-CH=N-), 6.8315-8.0939 multiplate (16H) (Ar-H)

3.2. Preparation of 2- { 4 - [2 - { 3,5bis (4-methoxyphenyl) - 4,5-dihydro-pyrazol-1-yl} – 2 - oxo ethoxy]phenyl} – 3 -(substitutedphenyl)-1,3-thiazolidin-4-one (2a-j)

A solution of compound N-[{4-[2-{3,5bis (4-methoxyphenyl)-4,5-dihydro-pyrazol-1-yl}-2-xoethoxy]phenyl}methylene] naphthalen-1-aniline (0.01M), thioglycolic acid (0.01M) and anhydrous zinc chlorid (2g) in absolute ethanol(60ml) was refluxed for 8 hours, concentrated, cooled and poured into the crushed ice and the filtered. The product obtained was purifed by recrystallization from acetone.

IR ; 2-a (cm^{-1})**:** 3010(=CH-), 2928 (-CH- stretch), 1717 (>C=O stretch),1679 (C=N-), 1599(>C=C< aromatic), 1440 (-CH_2- bend), 1375(-CH_3- bend), 1263 (C-N) 1220 (-N-N-), 1120(-C-O-C), 700 (C-S-C).

^{1}H NMR (DMSO);2-i: 2.5580, doublet (2H) (CH_2 -cyclic), 3.3840, singlet (2H) (-CH_2-), 3.7606, singlate (6H) (-OCH_3-), 4.8651, singlet (2H) (-CH_2-), 4.9943 triplet (1H) (-CH-) 5.9141, singlet (1H) (-CH-N<), 6.7401-8.1004 multiplate (16H) (Ar-H)

Table1. *Physical constant of 2-{4-[2-{3,5-bis(4-methoxyphenyl)-4,5-dihydro-pyrazol-1-yl}-2-xoethoxy]phenyl}-3-(substitutedphenyl)-1,3-thiazolidin-4-one*

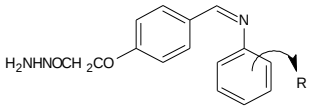
Sr. No.	Sample No.	R	Molecular Formula	Molecular Weight	Melting Point C	Yield	% C		% H		% N	
							Found	Required	Found	Required	Found	Required
1	2a	1-PHENYL	$C_{33}H_{31}N_3O_5S$	593.69	113	75	68.75	68.78	5.23	5.26	7.04	7.08
2	2b	1-AMINO	$C_{36}H_{33}N_3O_5S$	643.75	119	70	70.88	70.9	5.14	5.17	6.5	6.53
3	2c	4-CH_3	$C_{35}H_{33}N_3O_5S$	607.72	121	65	69.14	69.17	5.44	5.47	6.88	6.91
4	2d	3-CH_3	$C_{35}H_{33}N_3O_5S$	607.72	103	71	69.15	69.17	5.45	5.47	6.87	6.91
5	2e	2-NO_2	$C_{34}H_{30}N_4O_7S$	638.69	98	66	63.9	63.94	4.71	4.73	8.73	8.77
6	2f	3-NO_2	$C_{34}H_{30}N_4O_7S$	638.69	126	60	63.91	63.94	4.7	4.73	8.75	8.77
7	2g	4-NO_2	$C_{34}H_{30}N_4O_7S$	638.69	119	58	63.9	63.94	4.69	4.73	8.74	8.77
8	2h	2-Cl	$C_{34}H_{30}ClN_3O_5S$	628.14	115	72	64.98	65.01	4.78	4.81	6.65	6.69
9	2i	3-Cl	$C_{34}H_{30}ClN_3O_5S$	628.14	108	68	64.97	65.01	4.76	4.81	6.64	6.69
10	2j	4-Cl	$C_{34}H_{30}ClN_3O_5S$	628.14	120	62	64.95	65.01	4.77	4.81	6.63	6.69

4. RESULTS AND DISCUSSION

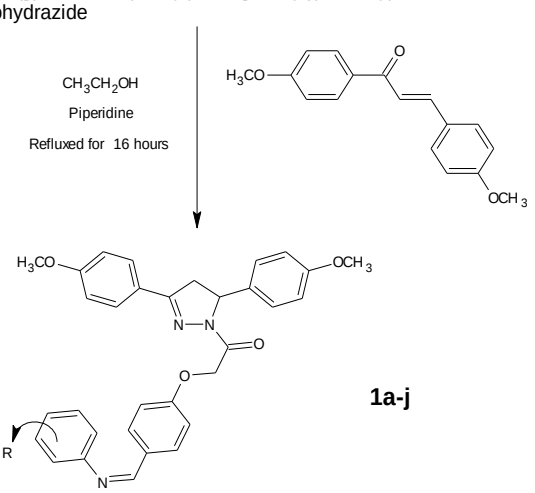
4.1. Antimicrobial Activity

The MICs of synthesized compounds were carried out by broth micro dilution method as described by Ratan (2000). The invitro antimicrobial activity of test compounds were assessed against 24 hr cultures of several selected bacteria and fungi. The bacteria used were *E. coli, S.aureus, P. aeruginosa*, and *S. pyogenus*; the fungi used were *C. albicans, A.niger, and A.clavatus.* The antimicrobial activity was performed by broth dilution method in DMSO. Gentamycin, Ampicilin ,Chloramphenicol, Ciprofloxacin, Norfloxacin, Nystatin and Greseofulvin were used as standard for the evaluation of antibacterial and antifungal activities respectively. The activity was reported byMinimal Inhibition Concentration. The results are summarized in Table-2.

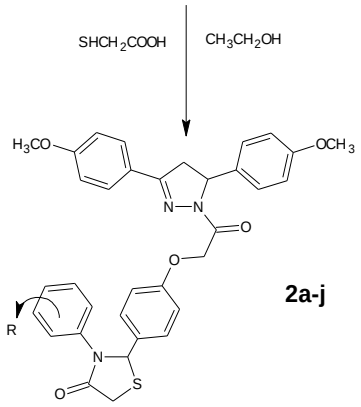
Reaction Scheme



2-(4-{[(substitutedphenyl)imino]methyl}phenoxy)ac
etohydrazide



N-[{4-[2-{3,5-bis(4-methoxyphenyl)-4,5-dihydro-pyrazol-1-yl}-
2-oxoethoxy]phenyl}methylene]substitutedaniline



2-{4-[2-{3,5-bis(4-methoxyphenyl)-4,5-dihydro-pyrazol-1-yl}-2-
oxoethoxy]phenyl}-3-(substitutedphenyl)-1,3-thiazolidin-4-one

Table2.*Antimicrobial activity of 2- { 4- [2 - { 3,5bis (4 – methoxyphenyl) - 4,5-dihydro-pyrazol-1-yl}-2-oxoethoxy]phenyl}-3-(substitutedphenyl)-1,3-thiazolidin-4-one*

SR. NO.	COMP. NO.	R	ANTIBACTERIAL ACTIVITY Minimal Inhibition Concentration (µg/ml)				ANTIFUNGAL ACTIVITY Minimal Inhibition Concentration (µg/ml)		
			Gram -Ve bacteria		*Gram +Ve bacteria*		*Fungus*		
			E.COLI	P.AERUGINOSA	S.AUREUS	S.PYOGENUS	C.ALBICANS	A.NIGER	A.CLAVATUS
			MTCC 443	MTCC 1688	MTCC 96	MTCC 442	MTCC 227	MTCC 282	MTCC 1323
1	2a	1-Phenyl	150	200	150	175	700	800	>1000
2	2b	1- Napthyl	125	100	200	200	800	600	800
3	2c	-4-CH_3	200	62.5	200	250	1000	>1000	>1000
4	2d	-3-CH_3	175	200	175	150	900	500	600
5	2e	-2-NO_2	200	100	175	100	600	700	500
6	2f	-3-NO_2	200	150	125	150	600	800	700
7	2g	-4-NO_2	175	125	150	175	800	800	800
8	2h	-2-Cl	150	200	175	200	900	900	500
9	2i	-3-Cl	125	150	125	150	700	500	700
10	2j	-4-Cl	175	150	200	100	>1000	800	900

Biological screening result of 2-{4-[2-{5-(4-chlorophenyl)-3-(4-methoxyphenyl)-4,5-dihydro-pyrazol-1-yl}-2-oxoethoxy]phenyl}-3-(substitutedphenyl)-1,3-thiazolidin-4-one based derivatives shows that compound (**2f,2i**) have shown better activity against E. coli, S. aureus, while rest of all compound possessed good activity against S.aureus in the range of 125-250 g/ml..Compounds with substitution 4-hydroxy (**2e** and **2j**), shown good antibacterial activity against S. pyogenus , while rest of all derivatives possessed good activity against S. pyogenus in the range of 100-250 g/ml.Compound (**2d)** and (**2e)** is found to be significant antifungal activity against C. albicans, while rest of all derivatives are poor against A.niger, and A.clavatus

5. CONCLUSION

The Main focus of this research work was to synthesize, characterize and evaluate antimicrobial activities of the newly synthesized Chalcone derivatives, structures of synthesized compounds were confirmed and characterized with the help of analytical data's such as IR and 1H-NMR. In summary, we have described the synthesis and antimicrobial activity of novel2-{4-[2-{3,5bis (4-methoxyphenyl)-4,5-dihydro-pyrazol-1-yl}-2-oxoethoxy]phenyl}-3-(substitutedphenyl)-1,3-thiazolidin-4-one substitute ed aniline MIC values revealed that amongst newly synthesized compound having 4-chlorophenyl type linkage has shown good activity against the bacterial strains. Rest of all compounds exhibit moderate improvement in activity against some of the pathogenic strains.

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REFERENCES

[1] T. Tomasic , L. P. Masic, *Curr. Med. Chem.*, 2009**,** 16, 1596.

[2] R. Lesyk, B. Zimenkovsky, D. Atamanyuk, F. Jensen, K. Kiec-Kononowicz, A. Gzell, *Bioorg. Med. Chem.*,2006,14,5230

[3] D. Havrylyuk, B. Zimenkovsky, O. Vasylenko, L. Zaprutko, A. Gzella, R. Lesyk, *Eur.J. Med. Chem.*, 2009, 44, 1396.

[4] D.Kaminskyy, B.Zimenkovsky, R. Lesyk, *Eur. J.Med.Chem.*, 2009, 44, 3627.

[5] R. Ottana, R. Maccari, M.L. Barreca, G. Bruno, A. Rotondo, A. Rossi, G. Chiricosta, R. Di Paola, L. Sautebin, S. Cuzzocrea, M.G. Vigorita, *Bioorg. Med. Chem.*, 2005, 13, 4243.

[6] P. Vicini, A. Geronikaki, K. Anastasia, M. Incerti, F. Zani, *Bioorg. Med. Chem.*, 2006, 14, 3859.

[7] A.A. Elbarbary, A.I. Khodair, E.B. Pedersen, C. Nielsen, *Monatsh. Chem.*, 1994, 125, 593.

[8] E. Rydzik, A. Szadowska, A. Kaminska, *Acta Pol. Pharm.*, 1984, 41, 459-464.

[9] H.L. Liu, Z.C. Li, T. Anthonsen, *Molecules*, 2000, 5, 1055.

[10] B. Samir, K. Wesam, A.F. Ahmed, *Eur. J. Med. Chem.*, 2007, 42, 948.

[11] (a) V. Vanheusden, H. M. Lehmann, M. Froeyen, L. Dugue, J. A. Heyerick, D. De Keukeleire, S. Pochet, R. Busson, P. Herdewijn, S. Van Calenbergh, *Med. Chem*., 2003, 46, 3811; (b) T. S. Lin, J. L. Zhu, G. E. Dutschman, Y. C. Cheng, W. H. Prusoff, *J. Med. Chem*., 1993, 36, 353.

[12] Rao A, Chimirri A, Ferro S, Monforte AM, Monfort P, Zappala M.Microwave- assisted synthesis of benzimidazole and thiazolidinone derivatives as HIV-1 RT inhibitors. Arkivoc 2004; 5: 147-155.

[13] Murugesan V, Prabhakar YS, Katti SB. CoMFA and CoMSIA studies on thiazolidin-4-one as anti-HIV-1 agents, J. Mol. Graph.Model. 2009; 27 (6): 735- 743.

[14] Balzarini J, Krzesinsk BO, Maeerin JK, Orzesko A. Synthesis and anti-HIV studies of 2- and 3-adamantyl-substituted thiazolidin- 4-ones. Eur. J. Med. Chem. 2009; 44 (1): 303-311.

[15] Diurno MV, Mazzoni O, Izzo AA, Bolognese A. Synthesis and pharmacological activity of 2-(substituted phenyl)-3-[2 or 3-[(4-substituted phenyl-4-hydroxy) piperidino] ethyl or propyl]-1,3-thiazolidin-4-ones. Farmaco 1997; 52 (4): 237-41.

[16] Diurno MV, Mazzoni O, Correale G, Monterry IG. Synthesis and structure- activity relationships of 2-(substituted phenyl)-3-[3-(dimethylamino)propyl]-1,3-thiazolidin-4-ones acting as H1-histamine antagonists. Farmaco 1999; 54 (9): 579-83.

[17] Kato T, Ozaki T, Tamura K. Novel calcium antagonists with both calcium overload inhibition and antioxidant activity. 2. Structure-activity relationships of thiazolidinon derivatives. J. Med. Chem.1999; 42 (16): 3134-46.

[18] Kato T, Ozaki T, Ohi N. Improved synthetic methods of CP-060S, a novel cardio protective drug. Tetrahedron Asymmetry 1999; 10: 3963-68.

[19] Adachi Y, Suzuki Y, Homma N, Fukazawa M, Tamura K, Nishie I,Kuromaru O. The anti-ischemic effects of CP-060S during pacing-induced ischemia in anesthetized dogs. Eur. J. Pharmacol. 1999; 367: 267-73.

[20] Tanabe Y, Yamamoto H, Murakami M, Yanagi K, Kubota Y, Okumura H, Sanemitsu Y, Suzukamo G. Synthetic study of the highly potent and selective anti-platelet activating factor thiazolidin-4-one agents and related compounds. J. Chem. Soc.Perkin Trans. 1995; 1: 935 -47.

[21] Kato Y, Kita Y, Nishio M, Hirasawa Y, Ito K, Yamanaka T,Motoyama Y, Seki. In vitro antiplatelet profile of FR171113, a novel non-peptide thrombin receptor antagonist. Eur. J.Pharmacol. 1999; 384: 197-202.

[22] Voss ME, Carter PH, Tebben AJ, Scherle PA, Brown GD,Thompson LA, Xu M, Lo YC, Yang-Liu RRQ. Both 5-arylidene-2-thioxodihydropyrimidine-4,6(1H,5H)- diones and 3-thioxo-2,3-dihydro-1H-imidazo[1,5-a]indol-1-ones are light- dependent tumor necrosis factor-alpha antagonists. Bioorg. Med. Chem. Lett. 2003; 13(3): 533-38.

[23] Mithlesh, Pareek PK, Chippa H, Kant R, Ojha KG. Microwave synthesis of new biologically important 1, 4-dihydropyridines containing benzothiazole moiety. Collection of Czechoslovak Chemical Communications 2010; 75(3): 275-87.

[24] Pareek PK, Mithlesh, Pareek D, Chaudhary M, Pareek A, Kant R, Ojha KG. Rapid synthesis of some medicinally important hexahydro-s-triazine derivatives incorporating benzothiazole moiety. Main Group Chemistry 2011; 10: 63-71

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