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Novel Substituted 4-Thiazolidinone, Synthesis and Antimicrobial Evaluation

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ABSTRACT *A series of novel 4-thiazolidinone were synthesized with the aim to synthesize the biologically active molecules via C condensation of Schiff bases and thioglycolic acid. These newly synthesized compounds were characterized by physical, chemical and spectral analysis data (IR, 1H-NMR, Mass) and are further screened for their antimicrobial activity using different Antimicrobes.*

KEYWORDS : Amlodipine Schiff bases, substituted4-thiazolidinones, Antimicrobial Activity

Introduction

In medicinal chemistry, 4-thiazolidinone has received an important role due to wide variety of physiological activities. A compound with biological activity is often derived from heterocyclic structure. Indeed one of the richest sources of diversity for the medicinal chemistry is small heterocyclic ring, which in addition to often exhibiting biological activity, may serve as rigid scaffolds for further display of functionalities.

In recent years, interests of researchers have been focused on the heterocyclic systems which contain various heteroatoms such as nitrogen, sulphur and oxygen, because of their biological importance.

4-Thiazolidinone derivatives have been demonstrated to act as antibacterial [1-10] and antiprotozoal [2], antifungal [11-14], anticonvulsant [15-19], anticancer [20-21], antituberculosis [22-28], antitumor [29-30] and ant parasitic, herbicidal agents [31-35], anti-inflammatory [36], and analgesic [37].

Literature survey shows that, 4-thiazolidenone of amlodipine Schiff bases are not synthesized and studied for their antimicrobial properties. Hence the present study was undertaken with the aim to synthesis new 4-thiazolidenones from amlodipine Schiff bases and studied their antimicrobial activities against different pathogens

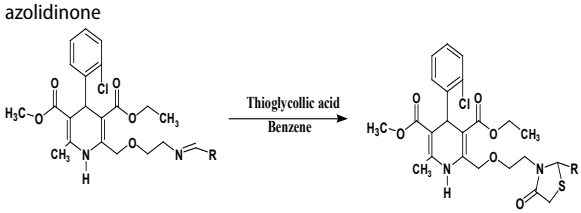
Materials and methods

Experimental

Melting points were uncorrected and determined in open capillaries. The purity of the compound is checked by TLC. The IR spectra were recorded on FTIR Shimadzu spectrometer, and ^{1}HNMR spectra were recorded on a Varian 300 MHz spectrometer ($CDCl_3$) using TMS as an internal standard. Mass spectra were recorded on VG 70704 mass spectrometer at 70 ev.

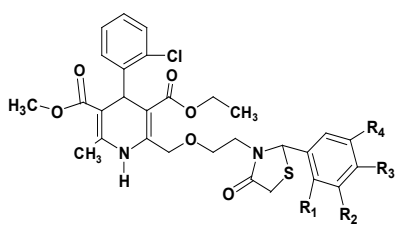
Synthesis of Thiazolidinones:

To a solution of imine (1.0 gm, 0.001mol) in dry benzene was added thioglycollic acid (0.18 gm, 0.001mol).The contents were refluxed for 6h until completion of the reaction. Excess solvent was removed under reduced pressure and the residue was treated with saturated solution of $NaHCO_3$, extracted with ethyl acetate, dried with Na_2SO_4 and solvent was distilled off. The residue on re-crystallization gave 4-thiazolidinone



Amlodipine Schiff bases Amlodipine Thiazolidinones

Where **R** is the substituted benzaldehyde



(3a-I)

The compounds (**3a-l)** were prepared by using the above procedure and their percentage yield and physical constants were recorded in Table II. Their structures have been confirmed by Mass, IR and ^{1}HNMR spectra.

Table I: Physical data of the compounds (3a-l)

Comp. No.	R_1	R_2	R_3	R_4	Yield (%)	M. P. (°C)
3a	H	H	OCH_3	OCH_3	78	165-167
3b	H	H	OH	NO_2	79	113-115
3c	H	H	Br	OCH_3	58	126-129
3d	H	H	F	Br	48	150-152
3e	H	H	H	Cl	86	102-104
3f	Cl	Cl	H	H	72	178-180
3g	H	H	H	F	59	137-142
3h	NO_2	H	H	H	65	142-144
3i	Cl	H	H	H	66	134-136
3j	H	H	F	H	60	112-114
3k	H	NO_2	H	Br	61	127-129
3l	Br	H	H	H	68	172-174

Spectral analysis:

Compound (3i):

^{1}HNMR: ^{1}HNMR spectra were recorded in DMSO- d_6 on a Varian AS instrument at 400 MHz using TMS as an internal standard.

(DMSO) δ **ppm:**1.09 (t, 3H, CH_3);2.5(s, 3H, CH_3); 2.85(m, 2H,CH_2);3.5(s, 3H, $0CH_3$);3.52(dd, 2H, CH_2); 3.8(dd, 2H, CH_2);3.97(m , 2H, CH_2 methylene protons); 4.5(dd, 2H, CH_2); 5.27(s, 1H, CH);6.18(s, 1H ,thiazolidinone proton);7.0-7.7(m, 8H, aromatic proton); 8.49(s, 1H, N-H)

(DMSO+D_2O) δ **ppm:**1.09 (t, 3H, CH_3);2.5(s, 3H, CH_3);3.0(m, 2H ,CH_2); 3.5(s, 3H, $0CH_3$); 3.7(dd, 2H, CH_2); 3.8(dd, 2H, CH_2); 3.97(m , 2H, CH_2methylene protons); 4.5(dd, 2H, CH_2); 5.24(s, 1H, CH);6.10(s, 1H ,thiazolidinone proton); 7.0-7.5(m, 8H, aromatic proton).

I.R.: IR spectra were recorded in KBr disc on Shimadzu FT-IR 8300 spectrophotometer.

3318(NH);1714,1697 and 1649 (C=O).

Mass: Mass spectra were recorded on Water-Macromass Quattro-ll mass spectrometer.

Mass (m/z) 605 (M+1)

Compound (3l):
(DMSO) δ **ppm:**1.06 (t, 3H, CH_3);2.2(s, 3H, CH_3); 2.9(m, 2H ,CH_2);3.5(s, 3H.OCH_3); 3.7(dd, 2H, CH_2); 3.8(dd, 2H, CH_2); 3.97(m , 2H, CH_2 methylene protons); 4.5(dd, 2H, CH_2); 5.27(s, 1H, CH);6.18(s, 1H ,thiazolidinone proton); 7.0-7.5(m, 8H, aromatic proton); 8.4 9(s, 1H, N-H)

(DMSO+D_2O) δppm**:**1.09 (t, 3H, CH_3);2.5(s, 3H, CH_3); 3.0(m, 2H ,CH_2);3.5(s, 3H, $0CH_3$);3.7(dd, 2H, CH_2); 3.8(dd, 2H, CH_2); 3.97(m , 2H, CH_2methylene protons); 4.5(dd, 2H, CH_2); 5.24(s, 1H, CH);6.10(s, 1H ,thiazolidinone proton); 7.0-7.5(m, 8H, aromatic proton).

I.R. (cm^{-1}): 3298(NH); 1726, 1684 and 1656(C=O).

Mass: Mass (m/z) 648.9 (M+1)

Compound: 3h
(**$CDCl_3$**) δppm**:**1.19 (t, 3H, CH_3);2.38(s, 3H,CH_3); 3.0(m, 2H ,CH_2);3.6(s, 3H, $0CH_3$); 3.7(dd, 2H, CH_2); 3.8(dd, 2H, CH_2); 3.97(m , 2H, CH_2methylene protons); 4.5(dd, 2H, CH_2); 5.4(s, 1H, CH);5.8(s, 1H ,thiazolidinone proton); 7.0-8.2(m, 8H, aromatic proton); 8.4 9(s, 1H, N-H)

($CDCl_3$+D_2O) δppm**:**1.09 (t, 3H, CH_3);2.5(s, 3H, CH_3);3.0(m, 2H ,CH_2);3.5 (s, 3H, OCH_3);3.7(dd, 2H, CH_2); 3.8(dd, 2H- CH_2); 3.97(m , 2H, CH_2methylene protons); 4.5(dd, 2H, CH_2); 5.24(s, 1H, CH);6.10(s, 1H ,thiazolidinone proton);7.0-8.2(m, 8H, aromatic proton).

I.R. (cm^{-1}): 3320(NH); 1703, 1684 and 1655(C=O).

Mass: Mass (m/z) 616 (M+1)

Compound-3f
($CDCl_3$) δppm**:**1.18 (t, 3H, CH_3);2.38(s, 3H, CH_3); 3.1(m, 2H, CH_2);3.6(m, 5H, $0CH_3$-CH_2); 3.8(dd, 2H, CH_2); 3.97(m , 2H, CH_2methylene protons); 4.5(dd, 2H, CH_2); 5.4(s, 1H, CH);6.1(s, 1H ,thiazolidinone proton);7.0-7.4(m, 7H, aromatic proton); 7.5(s, 1H, N-H)

I.R.: IR spectra were recorded in KBr disc on Shimadzu FT-IR 8300 spectrophotometer.

(3f) (cm^{-1})**:**3334(N-H),1725,1697.7 and 1652.3(C=O).

Mass: Mass (m/z) 639 (M+1)

Antimicrobial activity

Antimicrobial screening was done by using cup plate method (38-39) concentration of 100µg/ml. The compounds were evaluated for antibacterial activity against Bacillus subtilis gr +ve, Pseudomonas aeruginosa gr –ve , Staphylococcus aureus gr +ve, Escherichia coli gr –ve and antifungal activity against Aspergillus niger, Aspergillus Flavus, Curvularia, Alternaria. DMSO was used as solvent control. The results of antimicrobial data are summarized in **Table 2.** All compounds show the moderate to good activity against bacterial and fungal strain.

Table II: Antimicrobial screening of Compounds (3a-i)

Products	Bacteria (Zone of Inhibition in mm)				Fungi (Zone of Inhibition in mm)			
	A	B	C	D	E	F	G	H
I	12	16	12	---	---	17	---	14
II	11	12	13	---	---	14	16	17
III	12	18	21	---	14	---	16	---
IV	12	20	14	15	---	---	17	13
V	15	21	12	14	---	13	17	18
VI	12	16	13	---	---	---	15	17
VII	15	12	14	11	14	17	---	18
VIII	14	17	11	19	15	---	21	---
IX	14	11	21	10	---	13	---	14
X	11	11	14	18	12	---	17	---

A= *Bacillus subtilis gr +ve*, B= *Pseudomonas aeruginosa gr –ve,* C= *Staphylococcus aureusgr +ve,* D= *Escherichia coli gr –ve., E= Aspergillus niger, F= Aspergillus Flavus, G= Curvularia, H= Alternaria*

CONCLUSION

In conclusion, here we have reported some novel 4-thiazolidinone were synthesized via condensation of amlodipine Schiff bases and mercaptopropionic acid in dry benzene at refluxing temperature. The newly synthesized 4-thiazolidinone were confirmed by spectral analysis and further evaluated for their antimicrobial activity. The antibacterial and antifungal activity revealed that most of the compounds showed moderate to good activity.

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