WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.074
Volume 7, Issue 16, 658-667. Research Article ISSN 2277– 7105

SYNTHESIS, CHARACTERISATION AND BIOLOGICAL EVALUATION OF HETEROCYCLES CONTAINING BIS-THIAZOLIDINE RING USING HALOVINYL ALDEHYDES

Javed Hanif Mansoory[1] and Shankarsing Sardarsing Rajput*[2]

[1]Department of Chemistry, PSGVPM's Arts, Commerce and Science College, Shahada, Distt. Nandurbar (MS) India 425409.

[*2]Department of Chemistry, SVS's Dadasaheb Rawal College Dondaicha, Distt. Dhule (MS) India 425408.

Article Received on
26 June 2018,

Revised on 16 July 2018,
Accepted on 06 August 2018,

DOI: 10.20959/wjpr201816-12775

***Corresponding Author**
Shankarsing Sardarsing Rajput
Department of Chemistry, SVS's Dadasaheb Rawal College Dondaicha, Distt. Dhule (MS) India 425408.

ABSTRACT

A series of novel bis-thiazolidine derivatives with pyrrole ring was designed and synthesized. N-phenyl succinimide on haloformylation with Vilsmeier-Haack reagent (DMF/$POCl_3$) furnished halovinyl aldehyde which on condensation with *l*-cysteine afforded the target compounds in catalytic amount of piperdine**.** The synthesized compounds were characterised by spectral analysis. Biological screening shows some of the synthesized compounds exhibit good anti-microbial activity.

KEYWORDS: Bis-thiazolidine, halovinyl aldehydes, di-halo formy lation, DMF/$POCl_3$.

INTRODUCTION

Heterocyclic chemistry is an important class of synthetic organic chemistry. Heterocyclic compounds are of great importance biologically as well as industrially. Moreover, these are also useful to both developed and developing human society. Nearly all of the synthetic pharmaceutical products that are identical to natural products in the view of biological activity are heterocycles. The Vilsmeier-Haack reaction is widely used for halo-formylation.[1] Halo-formylation is an important step in organic synthesis. It results in introduction of a halogen and an aldehyde function (-CHO), which can be used for preparation of various types of functionalized compounds. So a variety of methods have been developed for halo-formylation reaction.[2-4]

A large number of drugs and biologically relevant molecules contain heterocyclic systems. Among these heterocyclic systems, thiazolidine is a biologically important compound known to be associated with several biological activities.

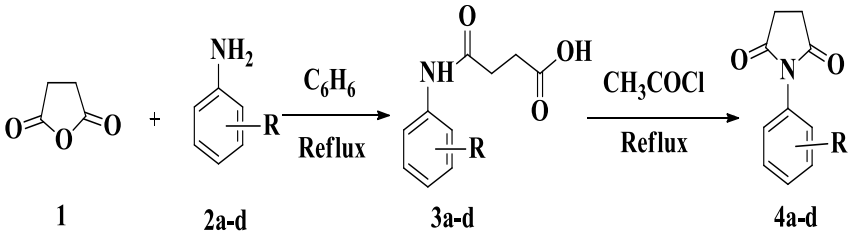
Thiazolidine is a five membered saturated ring containing an atom of sulphur at position 1 and an atom of nitrogen at position 3 as ring constituents. The chemistry of thiazolidine ring systems is of considerable interest because it is a core structure in various synthetic drugs and pharmaceutical products showing all types of biological activities like anti-microbial[5-7], anti-bacterial[8,9], anti-fungal[10-12], fungicidal[13], herbicidal[14], anti-malarial[15], anti-viral[16], anti-HIV[17], analgesic[18], anti-inflammatory (COX-inhibitors)[19], anti-tumor[20,21], anti-cancer[22,23], anti-tubercular[24], anti-proliferative[25], anti-diuretic[26], anti-convulsant[27], anti-histaminic(H1-antagonist)[28], Ca^{2+} channel blocker[29], cardio protective[30] properties. This diversity in the biological activities of thiazolidine has attracted the attention of many researchers to explore its multiple potential against several activities.

MATERIALS AND METHODS

Experimental

All chemicals, reagents and solvents used for synthesis of compounds, are of commercial grade. Melting points were determined in open capillary and are uncorrected. IR spectra were recorded using KBr discs on a Shimadzu FT-IR PC spectrophotometer. ^{1}HNMR spectrum were recorded on Bruker DRX 500MHz NMR spectrometer with DMSO-d_6 as a solvent using TMS as internal reference (chemical shift in δ ppm). Chemical shift were recorded as values in part per millions (ppm). The reactions were monitored by TLC. All these compounds were synthesized according to following scheme I, II and III.

General procedure for the synthesis of N-substituted phenyl succinimides (4a-d): succinic anhydride **1** (0.01mol) in 30 mL of benzene treated with substituted aniline **2a-d** (0.01mol) in 10 mL of benzene slowly for 3 hours, to obtained N-substituted succinamic acid **3a-d**. This compound **3** was cyclised with acetyl chloride (0.06mol) till complete evaluation of hydrogen chloride gas (**Scheme I**). The product **4** obtained was cooled, recrystallized from ethanol.



Where R_1, a = H, b = 4-Cl, c = 4-Me, d = 3-NO_2

Scheme I

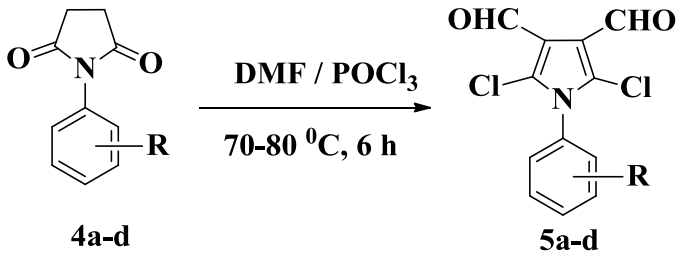
1-phenylpyrrolidine-2,5-dione (4a): M.F. $C_{10}H_9O_2N$, M.P. 156-158°C, FT-IR (ν, cm^{-1}KBr disc): 2927 (-CH_2), 1699.9 (>C=O), 1476 (Ar-C=C), 1204 (C-N), 820 (C-Cl). ^{1}HNMR (500MHz, DMSO-d_6): 2.9δ (s, 4H, -CH_2CH_2), 8.1-6.9δ (m, 5H, Ar-H).

1-(4-chlorophenyl)pyrrolidine-2,5-dione (4b): M.F. $C_{10}H_8O_2NCl$, M.P. 160-162°C, FT-IR (ν, cm^{-1} KBr disc): 2936 (-CH_2), 1703 (>C=O), 1507 (ArC=C), 1242 (C-N). ^{1}HNMR (500MHz, DMSO-d_6): 2.3δ (s, 4H, -CH_2CH_2), 8.5-7.4δ (m, 4H, Ar-H).

1-p-tolylpyrrolidine-2,5-dione (4c): M.F. $C_{11}H_{11}O_2N$, M.P. 158-160°C, FT-IR (ν, cm^{-1} KBr disc): 2924 (CH_2), 1702 (>C=O), 1419 (ArC=C), 1202 (C-N). ^{1}HNMR (500MHz, DMSO-d_6): 2.8-2.7δ (s, 4H, -CH_2CH_2), 3.16δ (s, 3H, -CH_3), 7.5- 6.9δ (m, 4H, Ar-H).

1-(4-nitrophenyl)pyrrolidine-2,5-dione (4d): M.F. $C_{10}H_8O_4N_2$, M.P. 180-182°C, FT-IR (ν, cm^{-1} KBr disc): 2933 (CH_2), 1706 (>C=O), 1511 (ArC=C), 1252 (C-N). ^{1}HNMR (500MHz, DMSO-d_6): 2.3δ (s, 4H, -CH_2CH_2), 7.5-7.1δ (m, 4H, Ar-H).

Synthesis of 2,5-dichloro-1-(substituted phenyl)-1H-pyrrole-3,4-dicarbaldehyde (5a-d): To a cooled dimethylformamide (0.24mol), freshly distilled phosphorus oxychloride (0.12mol) was slowly added in a drop wise fashion with constant stirring at 5-10°C. Then the succinimide **4a-d** (0.02mol) was slowly added to a cooled Vilsmeier-Haack reagent in small aliquots at a time with constant stirring using magnetic stirrer. This reaction mixture was heated at 60-70°C for 6 hours (**Scheme II**). This mixture was kept overnight and was then slowly added to crush ice with stirring and stirred for another 30 minutes. Then the resulting clear coloured solution was neutralised with 40% sodium hydroxide maintaining the temperature below 50°C. The reaction mixture was then heated at 50-60°C for 30 minutes. After cooling in an ice bath coloured compounds were obtained. These compounds were recrystallized with aqueous methanol.



4a-d **5a-d**

R_1, a = H, b = 4-Cl, c = 4-Me, d = 3-NO_2

Scheme II

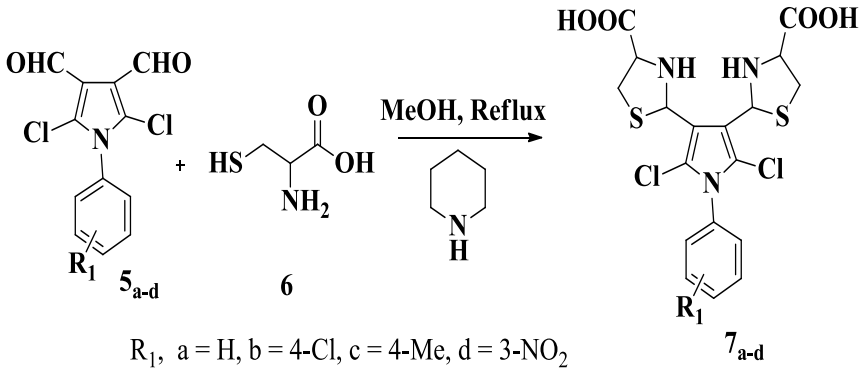
2,5-dichloro-1-phenyl-1H-pyrrole-3,4-dicarbaldehyde (5a): M.F. $C_{12}H_7O_2NCl_2$, M.P. 110-112^oC, FT-IR (ν, cm^{-1} KBr disc): 2820(-CHO), 1700.40(>C=O), 1475.11(Ar=C), 1311.14(C-N), 812.81(C-Cl). ^{1}HNMR (500MHz, DMSO-d_6): 8.3-7.2δ (m, 3H, Ar), 10.9δ (s, 1H, -CHO).

2,5-dichloro-1-(4-chlorophenyl)-1H-pyrrole-3,4-dicarbaldehyde (5b): M.F. $C_{12}H_6O_2NCl_3$, M.P. 148-150^oC, FT-IR (ν, cm^{-1} KBr disc): 2850(-CHO), 1700(>C=O), 1501(ArC=C), 1184(C-N). ^{1}HNMR (500MHz, DMSO-d_6): 7.6-7.0δ (s, 4H, Ar-H), 9.43δ (s, 1H, -CHO).

2,5-dichloro-1-p-tolyl-1H-pyrrole-3,4-dicarbaldehyde (5c): M.F. $C_{13}H_9O_2NCl_2$, M.P. 114-116^oC**,** FT-IR (ν, cm^{-1} KBr disc): 2835(-CHO), 1705(>C=O), 1507(ArC=C), 1187(C-N). ^{1}HNMR (500MHz, DMSO-d_6): 3.3δ(s, 3H, -CH_3), 7.68-6.9δ (m, 3H, Ar-H), 10.1δ (s, 1H, -CHO).

2,5-dichloro-1-(4-nitrophenyl)-1H-pyrrole-3,4-dicarbaldehyde (5d): M.F. $C_{12}H_6O_4N_2Cl_2$, M.P. 158-160^oC, FT-IR (ν, cm^{-1} KBr disc): 2860(-CHO), 1705.93(>C=O), 1507.61(ArC=C), 1187(C-N). ^{1}HNMR (500MHz, DMSO-d_6): 7.9-7.0δ (s, 4H, Ar-H), 9.64δ (s, 1H, -CHO).

Synthesis of 2,2'-(2,5-dichloro-1-substituted phenyl-1H-pyrrole-3,4-diyl)bis(thiazolidine-4-carboxylic acid) 6a-d: A mixture of substituted halovinyl aldehydes **5a-d** (0.001 mol) and *l*-cysteine **6** (0.002mol) in 10 mL of methanol containing a drop of piperidine was refluxed for 5-6 hours. The reaction mixture on cooling was filtered and the resulting compound **7a-d recrystallized** from ethanol (**Scheme III**).



R_1, a = H, b = 4-Cl, c = 4-Me, d = 3-NO_2

Scheme III

2,2'-(2,5-dichloro-1-phenyl-1H-pyrrole-3,4-diyl)bis(thiazolidine-4-carboxylic acid) (7a): M.F. $C_{18}H_{17}O_4N_3S_2Cl_2$, MP 138-140$^oC$, FT-IR (ν, cm^{-1} KBr disc): 2360-3012 (broad, acid OH), 1405,1496 (Ar=C), 3210-3425(N-H), 540-694(C-S), 1338 (C-N), 820(C-Cl). ^{1}HNMR (500MHz, DMSO-d_6): 3.3δ (d, 2H, -CH_2 of thiazolidine ring), 3.83δ (q, 1H, -CH of thiazolidine ring), 2.82δ (s, 1H, N-H of thiazolidine ring), 3.59δ (s, 1H,-CH of thiazolidine ring), 7.5-7.2δ (s, 5H, Ar-H), 9.9δ (s, 1H,-COOH). Elemental analysis: calculated for $C_{18}H_{17}O_4N_3S_2Cl_2$: C-45.57, H-3.61, N-8.86, Cl-14.95, S- 13.52%; Found: C- 44.85, H- 3.52, N- 8.46, Cl- 14.24, S- 13.06%.

2,2'-(2,5-dichloro-1-(4-chlorophenyl-1H-pyrrole-3,4-diyl)bis(thiazolidine-4-carboxylic acid) (7b): M.F. $C_{18}H_{16}O_4N_3S_2Cl_3$, MP 126-128$^oC$, FT-IR (ν, cm^{-1} KBr disc): 2330-3005 (broad acid -OH), 1410,1490 (Ar=C), 3220-3415(N-H), 545-690(C-S), 1332 (C-N), 825(C-Cl). ^{1}HNMR (500MHz, DMSO-d_6): 2.63δ (d, 2H, -CH_2 of thiazolidine ring), 2.61δ (q, 1H, -CH of thiazolidine ring), 3.35δ (s, 1H, N-H of thiazolidine ring), 3.5δ (s, 1H, -CH of thiazolidine ring), 7.62-7.29δ (dd, 2H, Ar-H), 10.15δ (s, 1H,-COOH). Elemental analysis: calculated for $C_{18}H_{16}O_4N_3S_2Cl_3$: C-42.49, H-3.17, N-8.29, Cl-20.90, S- 12.6%; Found: C-41.86, H- 3.04, N- 8.04, Cl- 20.46, S-12.32%.

2,2'-(2,5-dichloro-1-(4-methylphenyl-1H-pyrrole-3,4-diyl)bis(thiazolidine-4-carboxylic acid) (7c): M.F. $C_{19}H_{19}O_4N_3S_2Cl_2$, MP 148-150$^oC$, FT-IR (ν, cm^{-1} KBr disc): 2355-3005 (broad acid -OH), 1415,1486 (Ar=C), 3220-3410(N-H), 520-684(C-S), 1325(C-N), 825(C-Cl). ^{1}HNMR (500MHz, DMSO-d_6): 2.7δ (d, 2H, -CH_2 of thiazolidine ring), 2.5δ (q, 1H, -CH of thiazolidine ring), 2.9δ (s, 1H, N-H of thiazolidine ring), 3.3δ (s, 1H, -CH of thiazolidine ring) 2.3δ (s, 3H,CH_3-Ar)6.2δ (d, 1H), 7.29-7.27δ (dd, 2H, Ar-H), 8.81δ (s, 1H,-COOH).

Elemental analysis: calculated for $C_{19}H_{19}O_4N_3S_2Cl_2$: C-46.72, H- 3.92, N- 8.60, Cl- 14.52, S-13.14; Found: C- 46.12, H- 3.84, N- 8.56, Cl- 14.12, S-12.98%.

2,2'-(2,5-dichloro-1-(3-nitrophenyl-1H-pyrrole-3,4-diyl)bis(thiazolidine-4-carboxylic acid) (7d): M.F. $C_{18}H_{16}O_6N_4S_2Cl_2$, MP 176-178$^oC$, FT-IR (ν, cm^{-1} KBr disc): 2350-3025 (broad acid -OH), 1425,1486 (Ar=C), 3210-3425(N-H), 540-674(C-S), 1340 (C-N), 825(C-Cl). ^{1}HNMR (500MHz, DMSO-d_6): 3.0δ (d, 2H,-CH_2 of thiazolidine ring), 2.66δ (q, 1H,-CH of thiazolidine ring), 3.37δ (s, 1H, N-H of thiazolidine ring), 3.61δ (s, 1H,-CH of thiazolidine ring), 8.63-7.58δ (m, 4H, Ar-H), 10.53δ (s, 1H, -COOH). Elemental analysis: calculated for $C_{18}H_{16}O_6N_4S_2Cl_2$: C- 41.63, H- 3.11, N- 10.74, Cl- 13.65, S-12.35%; Found: C- 41.08, H-3.04, N- 10.26, Cl- 13.42, S-12.04%.

Biological Activity of synthesized thiazolidine derivatives 7a-d: The synthesized compounds **7a-d** were evaluated in-vitro for antimicrobial activity against *Staphylococus aureus* and *Escherichia coli* and antifungal activity against *Alterneria alternata* and *Aspergillus niger* at the concentration 1000 microgram/mL by paper disk diffusion method using dimethyl sulphoxide (DMSO) as solvent and nutrient agar was employed as culture media, the results were obtained in the form of clearing zone and were noted after the period of incubation (at 37 ^oC for 24-48 hours) and results arerepresented in table-I.

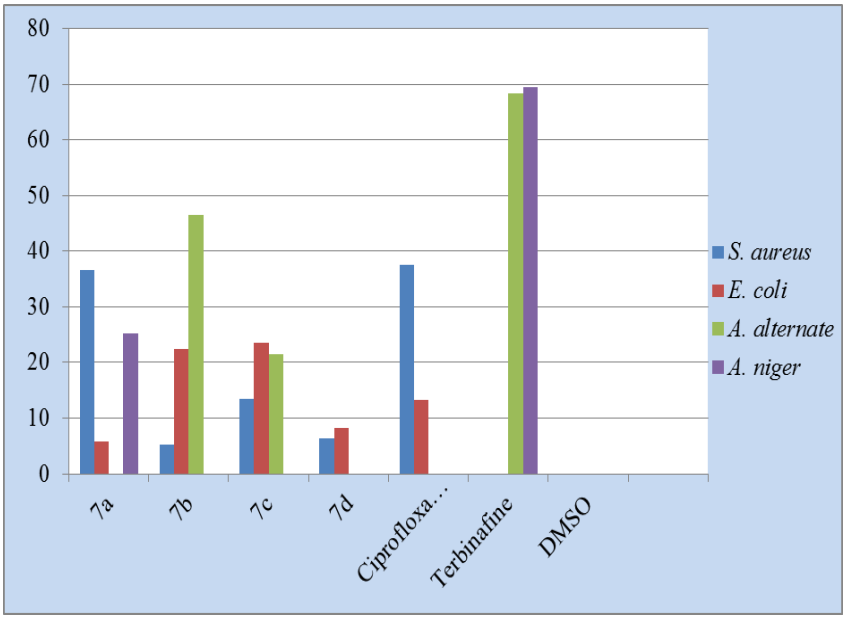
RESULT AND DISCUSSION

In summary, a new series of heterocyclic compounds with thiazolidine ring have been synthesized from halovinyl aldehydes and *l*-cysteine. And halovinyl aldehydes were synthesized from N-substituted phenyl succinimide on halo-formylation reaction with DMF/$POCl_3$. These aldehydes can be used for preparing different heterocycles. Halovinyl aldehydes are bi-functional derivatives capable of participating in a wide range of addition, substitution and cyclization reactions.Thiazolidine derivatives were synthesized from halovinyl aldehyde with *l*-cysteine and tested for biological activity. These derivatives showing moderate to good anti-bacterial activity (against *Staphylococus aureus* and *Escherichia coli*) and anti-fungal activity(against *Alterneria alternata* and *Aspergillus niger).*

Figures and Tables: The zones of inhibition were measured in mm and the data is presented in Table I.

Sr.	Compound	*S. aureus*	*E. coli*	*A. alternata*	*A. niger*
1	**7a**	36.52	5.73	-	25.23
2	**7b**	5.23	22.34	46.46	-
3	**7c**	13.36	23.52	21.54	-
4	**7d**	6.32	8.24	-	-
5	Ciprofloxacin (Positive control)	37.54	13.22	NA	NA
6	Terbinafine(Positive control)	NA	NA	68.28	69.52
7	DMSO(Negative control)	-	-	-	-

Diameter in millimeter calculated by Vernier caliper, '-' = no zone of inhibition, NA = Not applicable.



CONCLUSION

All compounds have been successfully synthesized and characterized by ^{1}HNMR and FT-IR spectroscopy techniques. Compounds 7a-d were screened for their in-vitro antimicrobial activity, compound 7a showed excellent activity against *Staphylococcus aureus* while compounds 7b and 7c showed good activity against *Escherichia coli.* In these compounds, 7b and 7c compounds were exhibited moderate and good activity against *Alterneria alternata* respectively and compound 7a showed good activity against *Aspergilus niger*.

ACKNOWLEDGEMENT

One of the authors is thankful to CSIR, New Delhi for their financial support (CSIR File No. 08/587/(0002)/2013-EMR-I Dated 14/07/2013). Authors are also thankful to Department of Chemistry and Department of Microbiology of PSGVPM's Arts, Commerce and Science

College, Shahada (MS) for providing research laboratory facility and microbial screening facility.

REFERENCES

1. Rajput AP, Rajput SS, Synthesis of benzaldehyde substituted phenyl carbonyl hydrazones and their formylation using Vilsmeier-Haack reaction. Int J Pharm Tech Res, 2009; 1(4): 1605-11.
2. Rajput AP, Rajput SS, Preparation and antimicrobial activity study of 2,5-dichloro-3,4-diformyl (N-substituted phenyl) pyrroles. Asian J Chem, 2007; 19(6): 4939-41.
3. Rajput SS, Synthesis, charactrisation and anti-bacterial activity of mercapto 1,2,4-triazole, 1,3,4-thiadiazoles, mercaptobenzhydrazones and thiazolidinone derivatives of 4-hydroxybenzhydrazide. Int J Pharm Pharm Sci, 2012; 4(2): 164-7.
4. Patil MM, Rajput SS, Synthesis and anti-microbial evaluation of 2,6-bis((E)-2-hydroxy naphthalen-1-yl) diazenyl)-1- substituted phenyl-1,4-dicarbaldehyde.World J Pharm Res, 2016; 5(10): 584-95.
5. Faidallah HM, Khan KA, Asiri AM, Synthesis and biological evaluation of new 3,5-di(trifluoromethyl)-1,2,4-triazolesulfonylurea and thiourea derivatives as antidiabetic and antimicrobial agents. J Fluor Chem, 2011; 132: 870–7.
6. Rajput SS, Mansoory JH, Synthesis, characterisation and biological evaluation of some novel Schiff's bases derived from halovinyl aldehyde and 4-amino-5-(pyridin-4-yl)-4H-1,2,4-triazole-3-thiol. Der Pharma Chemica, 2015; 7(10): 510-4.
7. Dhivare RS, Rajput SS, Microwave assisted synthesis and antimicrobial activities of 3,4-bis-(4-hydroxy-3-methoxy benzylidene)-7-(N-phenyl)-3,3a,3b,4,5,7-hexahydro-2*H*pyrrolo–[2,3-c,5,4-c]–dipyrazole. Int J Cur Trends Pharm Res, 2015; 3(6): 1111-4.
8. Rajput SS, Sayyed RM, Synthsis, characterization and biological evalution of 3,4-bis(substituted phenyl)-7-(2,6-dichloro-4- (trifluoromethyl) phenyl)-7*H*-pyrrolo[2,3-c:5,4-c"] diisoxazoles from 2,6-dichloro-4-trifluoro methyl aniline. Int J Cur Trends Pharm Res, 2017; 5(1): 10-5.
9. Rajput SS, Sayyed RM, Synthesis and evaluation of antimicrobial activity of some novel chalcones of 2,6-dichlori-4-trifluro methyl aniline. Hetero Lett, 2017; 7(2): 333-9.
10. Desai NC, Rajpara KM, Joshi VV, Microwave induced synthesis of fluorobenzamides containing thiazole and thiazolidine as promising antimicrobial analogs. J Fluor Chem, 2013; 145: 102-11.

11. Pareek PK, Mithlesh Kriplani P, Tiwari R, Ojha KG, Rapid synthesis and biological activities of some new benzothiazol-2-ylhexahydro-S-triazine derivatives. Phosphorus, Sulfur, Silicon, 2010; 185(7): 1338-45.
12. Rana PB, Mistry BD, Desai KR, Green chemistry: conventional and microwave induced synthesis of various thiazolidinone derivatives from 3-{[(1E)-(2'-chloro-7'-methoxyquinoline-3'-yl)methylene]amino}-4-(substitutedphenyldiazenyl) phenol and their antimicrobial screening. Arkivoc, 2008; 15: 262-79.
13. Xua X, Qianb X, Zhong L, Synthesis and fungicidal activity of fluorine-containing phenylimino-thiazolidines derivatives, J Fluorine Chem, 2005; 126: 297-300.
14. Li G, Qian X, Cui J, Huang Q, Cui D, Zhang R, Liu F, Synthesis and herbicidal activities of fluorine-containing 3-pyridylmethyl-2-phenyliminothiazolidine derivatives. J Fluorine Chem, 2006; 127: 182-6.
15. Vazzana I, Terranovaa E, Mattiolib F, Sparatorea F, Aromatic Schiff's bases and 2,3-disubstituted-1,3-thiazolidin-4-one derivatives as anti-inflammatory agents. Arkivok, 2004; 5: 364-74.
16. Ami E, Nakahara K, Sato A, Nguyen J-T, Hidaka K, Hamada Y, Nakatani S, Kimura T, Hayashia Y, Kisoa Y, Synthesis and antiviral property of allophenylnorstatine-based HIV protease inhibitors incorporating D-cysteine derivatives as P2/P3 moieties. Bioorg Med Chem Lett, 2007; 17: 4213-7.
17. Nagarajan SR, De CGA, Getman DP, Lu HF, Sikorski, Walker JL, Discovery of novel benzo-thiazole sulfonamides as potent inhibitors of HIV-1 protease. Bioorg Med Chem Lett, 2003; 11(22): 4769-77.
18. Kaur H, Kumar S, Singh I, Saxena KK, Kumar A, Synthesis, characterization and biological activity of various substituted benzothiazole derivatives. Digest J Nanomaterials Biostructures, 2010; 5(1): 67-76.
19. Paramashivappa R, Phani KP, Rao PVS, Rao S, Design, synthesis and biological evaluation of benzimidazole/benzothiazole and benzoxazole derivatives as cyclooxygenase inhibitors. Bioorg Med Chem Lett, 2003; 13(4): 657-60.
20. El-Gaby MSA, Ismail ZH, Abdel-Gawad SM, Aly HM, Ghorab MM, Synthesis of thiazolidine and thiophene derivatives for evaluation as anticancer agents. Phosphorus Sulfur Silicon Relat Elem, 2009; 184: 2645-54.
21. Beharry Z, Zemskova M, Mahajan S, Zhang F, Ma J, Xia Z, Lilly M, Smith CD, Kraft AS, Novel benzylidene-thiazolidine-2,4-diones inhibit Pim protein kinase activity and

induce cell cycle arrest in leukemia and prostate cancer cells. Mol Cancer Ther, 2009; 8: 1473-83.

22. Havrylyuk D, Mosula L, Zimenkovsky B, Vasylenko O, Gzella A, Lesyk R, Synthesis and anticancer activity evaluation of 4-thiazolidinones containing benzothiazole moiety. Eur J Med Chem, 2010; 45: 5012-21.
23. Onen-Bayram FE, Durmaz I, Scherman D, Herscovici J, Cetin-Atalay R, A novel thiazolidine compound induces caspase-9 dependent apoptosis in cancer cells. Bioorg Med Chem, 2012; 20: 5094-102.
24. Pareek D, Chaudhary M, Pareek PK, Kant R, Ojha KG and Pareek A Synthesis of some bioactive 4-thiazolidinone derivatives incorporating benzothiazole moiety. Der Chemica Sinica, 2010; 1(3): 22-35.
25. Li W, Lu Y, Wang Zhao, James T, Dalton, Miller D D, Synthesis and anti-proliferative activity of thiazolidine analogs for melanoma. Bioorg Med Chem Lett, 2007; 1: 4113-7.
26. Akhtar T, Saini B, Khan AR, Kumar A, Design and synthesis of benzylidene thiazolidine-2, 4- dione derivatives with their anticancer and anti-diabeticbiologial screening. 2014; 4(1): 1231-43.
27. Ergene N, Capan G, Synthesis and anticonvulsant activity of new 4-thiazolidone and 4-thiazoline derivatives. Farmaco, 1994; 49(6): 449-51.
28. Giorgioni G, Accorroni B, Stefano AD, Marucci G, Siniscalchi A, Claudi F, Benzimidazole, benzoxazole and benzothiazole derivatives as 5HT2B receptor ligands, synthesis and preliminary pharmacological evaluation. Med Chem Res, 2005; 14(2): 57-3.
29. Kato T, Ozaki T, Tamura K, Novel calcium antagonists with both calcium overload inhibition and antioxidant activity and Structure-activity relationships of thiazolidinone derivatives. J Med Chem, 1999; 42(16): 3134-46.
30. Kato T, Ozaki T, Ohi N, Improved synthetic methods of CP-060S, a novel cardioprotective drug. Tetrahedron Asymm, 1999; 10: 3963-8.