International Journal of Chemical, Materials and Biomolecular Sciences
ISSN: 2415-6620
Vol:8, No:12, 2014

Synthesis and Antimicrobial Profile of Newer Schiff Bases and Thiazolidinone Derivatives

N. K. Fuloria, S. Fuloria, R. Gupta

***Abstract*—**Esterification of p-bromo-m-cresol led to formation of 2-(4-bromo-3-methylphenoxy)acetate (1). 2-(4-Bromo-3-methyl phenoxy)acetohydrazide (2) is derived from Compound (1) by hydrazination. Compound (2) was reacted with different aromatic aldehydes to yield N-(substituted benzylidiene)-2-(4-bromo-3-methyl phenoxy)acetamide(3a-c). Cyclization of compound (3a-c) with thioglycolic acid yielded 2-(4-bromo-3-methylphenoxy)-N-(4-oxo-2-arylthiazolidin-3-yl) acetamide (4a-c). The newly synthesized compounds were characterized on the basis of spectral studies and evaluated for antibacterial and antifungal activities.

***Keywords*—**Imines, Thiazolidinone, Schiff base, Antimicrobial.

I. Introduction

THIAZOLIDINONES, imines and phenolic moieties are very well known to potentiate the antiviral [1], anticancer [2], [3], anti-tubercular [4], and antimicrobial [5]-[17] activities of organic molecules. As per the literary investigations, it was known that phenolic moieties can be converted into imines [17], [18]; which are precursors for thiazolidinones [19]-[23]. As per the literary reports azoles are particularly desirable structures for screening and are prevalent in drugs that have reached market place. Development of simple and general synthetic routes for widely used organic compounds from readily available reagents is one of major challenges to the organic chemists. To meet facile results of these tough challenges thiazolidinone nucleus was being considered. Among wide variety of heterocycles explored for developing pharmaceutical molecules, thiazolidinone derivatives played a vital role in medicinal chemistry. Hence, as per various reports, literature, prospects of antibiotics in global pharmaceutical market, also the activities associated with phenols, imines and thiazolidinones; an attempt was made to generate novel potent antimicrobials by converting phenolic ester moiety (1) into some novel 2-(4-bromo-3-methylphenoxy)-N-(4-oxo-2-arylthiazolidin-3-yl) acetamide(4a-e) via synthesis of hydrazide (2) and imines (3a-e) as key intermediates [23]. The novel compounds were further characterized and evaluated for their antimicrobial activities.

N. K. Fuloria is with the Faculty of Pharmacy, AIMST University, Semeling, Bedong, Kedah, Malaysia (corresponding author to provide phone: +60-164037685; e-mail: nfuloria@gmail.com).

S. Fuloria is with the Faculty of Pharmacy, AIMST University, Semeling, Bedong, Kedah, Malaysia (e-mail: shivani2jaju@gmail.com).

R. Gupta is with the R. V. Northland Institute of Pharmacy, Greater Noida, U. P., India (e-mail: rajulgupta01@yahoo.co.in).

II. Material and Methods

A. Material

Melting points of newly synthesized compounds were determined in open capillary tubes. IR spectra were recorded (in KBr) on Bruker PCIR, ^{1}HNMR spectra on Bruker, DPX 300 and mass spectra on MASPEC (MSW/9629) apparatuses. Purity of synthesized compounds was checked by TLC on aluminium sheets with silica gel 60 F_{254} (0.2 mm).

B. Methods

1. Synthesis of 2-(4-Bromo-3-MethylPhenoxy)Acetate (1)

A mixture of *p*-bromo-*m*-cresol (0.1mol), ethylchloroacetate (0.1mol) and anhydrous potassium carbonate (0.15mol) was refluxed for 16 hours. The resultant mixture was filtered and filtrate after distillation, was poured onto ice-cold water and stirred well. The obtained mixture was extracted with ether. The organic extract layer was dried and kept overnight with anhydrous sodium sulphate. Finally the dried organic mixture was purified under reduced pressure to yield pure compound (1). IR (KBr, cm-^{1}): 2994, 2928 (C-H), 1715 (C=O of ester), 1238 (C-O of ester). 1HNMR (CDCl3, δ ppm): 2.01 (3H, t, CH_3), 2.34 (3H, s, Ar-CH_3), 4.15 (2H, q, CH_2), 4.86 (2H, s, OCH_2), 6.50-7.04 (3H, m, Ar-H). MS (m/z): 272 (M^+), 274 (M^++2), 199 (base Peak), 185, 95. Anal.(Calcd.) Found: C (48.37) 48.35, H (4.80) 4.78.

2. Synthesis of 2-(4-Bromo-3-MethylPhenoxy)Aceto Hydrazide(2)

A mixture of ethyl aryloxyacetate (1) (0.05 mol) and hydrazine hydrate (0.075 mol) in ethanol was refluxed for 6 h. The reaction mixture was distilled to remove solvent and the crystals formed were recrystallized from methanol to yield pure compound (2). IR (KBr, cm-^{1}): 3275, 3284 (NH and NH2), 1742 (CO of ester), 1587, 1472, 1285, 1198, 1174, 1126, 1090, 864, 773 (C=C and C-H of aromatic ring). 1HNMR (CDCl3, δ ppm): 2.32 (3H, s, CH_3), 4.82 (2H, s, OCH_2), 5.62 (2H, br, NH_2), 6.52 (1H, d, J = 2.74 Hz, Ar-H2), 6.53 (1H, dd, J = 2.77, 6.31, 2.70 Hz, Ar-H6), 7.05 (1H, d, J = 6.68 Hz, Ar-H5), 9.52 (1H, s, NH). MS (m/z): 258 (M^+), 260 (M^++2), 185 (base Peak), 243, 242, 197, 95. Anal.(Calcd.) Found: C(41.72)41.69, H(4.28)4.24, N(10.81)10.78.

3. General Procedure for Synthesis of 2-{(4-Bromo-3-Methyl)Phenoxy}-N-[SubstitutedBenzylidiene]Aceto Hydrazides (3a-c):

A mixture of compound (2) (0.01 mol) and aromatic aldehyde (0.01 mol) in the presence of few drops of sulfuric acid was refluxed for 6 h. The product formed was isolated and recrystallized from methanol to yield compounds (3a-c).

a. N-(4-(dimethylamino)benzylidene)-2-(4-bromo-3-methyl phenoxy)acetohydrazide (3a)

IR (KBr, cm-1): 1645 (CO of CONH), 3214, 1632 (NH of CONH), 1594, 1471, 1296, 1190, 1166, 1121, 1081, 867, 836, 770 (C=C & C-H of aromatic ring). 1H-NMR (CDCl3, δ ppm): 2.39 (3H, s, CH_3), 2.87 (6H, s, $N(CH_3)_2$), 4.83 (2H, s, OCH_2), 6.51 (1H, d, *J* = 2.71 Hz, Ar-H2), 6.53 (1H, dd, *J* =2.74, 6.32, 2.71 Hz, Ar-H6), 6.62 (2H, d, *J* = 6.32Hz, Ar-H3& 5), 6.95 (2H, d, *J* = 6.96 Hz, Ar-H2 & 6), 7.04 (1H, d, *J* = 6.32 Hz, Ar-H5), 8.00 (1H, s, N=CH), 9.50. (1H, s, NH).MS (m/z) 390 (M^+), 392 (M^++2), 190 (base Peak), 243, 200, 186, 147, 120.Anal.(Calcd.) Found: C(55.39)55.36, H(5.16)5.14, N(10.77)10.73.

b. N-(4-chlorobenzylidene)-2-(4-bromo-3-methylphenoxy) acetohydrazide (3b)

IR (KBr, cm-1): 1647 (CO of CONH), 3258, 1627 (NH of CONH), 1591, 1465, 1292, 1160, 1130, 1082, 861, 836, 774 (C=C & C-H of aromatic ring). 1H-NMR (CDCl3, δ ppm): 2.35 (3H, s, CH_3), 4.90 (2H, s, OCH_2), 6.51 (1H, d, *J* = 2.81, Ar-H2), 6.54 (1H, dd, *J* = 2.76, 6.32, 2.74 Hz, Ar-H6), 7.04 (1H, d, *J* = 6.28 Hz, Ar-H5), 7.10 (2H, d, *J* = 6.32 Hz, Ar-H2 & 6), 7.21 (2H, d, *J* = 6.85 Hz, Ar-H3 & 5), 8.04 (1H, s, N=CH), 9.26 (1H, s, NH). MS (m/z): 381 (M^+), 383 (M^++2), 181 (base Peak), 366, 243, 200, 186, 138, 111. Anal.(Calcd.) Found: C (50.35) 50.31, H (3.70) 3.67, N (7.34) 7.30.

c. N-(2,4-dihydroxybenzylidene)-2-(4-bromo-3-methyl phenoxy) acetohydrazide (3c)

IR (KBr, cm-1): 1655 (CO of CONH), 3316, 1626 (NH of CONH), 3513, 3520 (OH on phenyl ring), 1594, 1448, 1288, 1197, 1178, 1158, 904, 798 (C=C & C-H of aromatic ring). 1H-NMR (CDCl3, δ ppm): 2.35 (3H, s, CH_3), 4.82 (2H, s, OCH_2), 5.18 (1H, s, OH), 5.28 (1H, s, OH), 6.21 (1H, d, *J* = 2.82 Hz, Ar-H3), 6.32 (1H, dd, *J* = 2.74, 6.73, 2.72 Hz, Ar-H5), 6.54 (1H, d, *J* = 2.73 Hz, Ar-H2), 6.55 (1H, dd, *J* = 2.68, 6.34, 2.68 Hz, Ar-H6), 7.07 (1H, d, *J* = 6.67 Hz, Ar-H5), 7.31 (1H, d, *J* = 6.67 Hz, Ar-H6), 8.11 (1H, s, N=CH), 9.18 (1H, s, NH) . MS (m/z): 379 (M^+), 381 (M^++2), 179 (base Peak), 364, 243, 200, 186, 136, 109. Anal.(Calcd.) Found: C (50.68) 50.65, H (3.99) 3.95, N (7.39) 7.38.

4. General Procedure for Synthesis of 2-(4-Chloro-3-Methyl Phenoxy)-N-(4-Oxo-2-Substituted ArylThiazolidin-3-yl)Acet Amides (4a-c)

A mixture of compound (3a-c) (0.01 mol) and thioglycolic acid (0.02 mol) in the presence of zinc chloride was refluxed for 12 h. The product formed was isolated and recrystallized from methanol to yield compounds (4a-c).

a.2-(4-bromo-3-methylphenoxy)-N-(2-(4-(dimethylamino) phenyl)-4-oxothiazolidin-3-yl)acetamide (4a)

IR (KBr, cm-1): 3255 (NH of CONH), 1760 (CO of Thiazolidinone ring), 1655 (CO of CONH), 1580, 1468, 1270, 1170, 1076, 878 (C=C & C-H of aromatic ring), 1148 and 697 (C-S of Thiazolidinone ring). 1H-NMR (CDCl3, δ ppm): 2.41 (3H, s, Ar-CH_3), 2.84 (6H, s, -$N(CH_3)_2$), 3.35 (2H, s, CH_2-S), 4.84 (2H, s, OCH_2), 5.85 (1H, s, -N-CH-S-), 6.44 (1H, d, *J* = 7.9 Hz, Ar-H3 & 5), 6.35 (1H, d, *J* = 2.8 Hz, Ar-H2), 6.48 (1H, dd, *J* = 2.9, 8.1 Hz, Ar-H6), 6.77 (1H, d, *J* = 8.3 Hz, Ar-H2 & 6), 7.06 (1H, d, *J* = 8.3 Hz, Ar-H5), 8.76 (1H, s, for NH). MS (m/z): 464 (M^+), 466 (M^++2), 243 (base peak), 449, 264, 221, 200, 186, 120. Anal.(Calcd.) Found: C(51.73)51.70, H(4.77)4.76, N(9.05)9.03.

b.2-(4-bromo-3-methylphenoxy)-N-(2-(4-chlorophenyl)-4-oxothiazolidin-3-yl)acetamide(4b)

IR (KBr, cm-1): 3260 (NH of CONH), 1750 (CO of Thiazolidinone ring), 1658 (CO of CONH), 1586, 1477, 1276, 1180, 1099, 870 (C=C & C-H of aromatic ring), 1140 and 680 (C-S of Thiazolidinone ring). 1H-NMR (CDCl3, δ ppm): 2.43 (3H, s, Ar-CH_3), 3.39 (2H, s, CH_2-S), 4.90 (2H, s, OCH_2), 5.93 (1H, s, -N-CH-S-), 6.39 (1H, d, *J* = 2.8 Hz, Ar-H2), 6.48 (1H, dd, *J* = 2.7, 8.1 Hz, Ar-H6), 7.04 (1H, d, *J* = 8.0 Hz, Ar-H2 & 6), 7.08 (1H, d, *J* = 8.2 Hz, Ar-H5), 7.20 (1H, d, *J* = 8.4 Hz, Ar-H3 & 5), 8.82 (1H, s, NH). MS (m/z): 455 (M^+), 457 (M^++2), 186 (base peak), 440, 255, 243, 212, 200, 111. Anal.(Calcd.) Found: C(47.44)47.42, H(3.54)3.52, N(6.15)6.12.

c.2-(4-bromo-3-methylphenoxy)-N-(2-(2,4-dihydroxy phenyl)-4-oxothiazolidin-3-yl)acetamide (4c)

IR (KBr, cm-1): 3525 (OH), 3248 (NH of CONH), 1770 (CO of Thiazolidinone ring), 1664 (CO of CONH), 1595, 1465, 1285, 1190, 1072, 894 (C=C & C-H of aromatic ring), 1138 and 691 (C-S of Thiazolidinone ring). 1H-NMR (CDCl3, δ ppm): 2.43 (3H, s, Ar-CH_3), 3.34 (2H, s, CH_2-S-), 4.85 (2H, s, O-CH_2), 5.34 (1H, s, 4-OH), 5.38 (1H, s, 2-OH), 5.87 (1H, s, -N-CH-S-), 6.15 (1H, d, *J* = 2.7 Hz, Ar-H2), 6.33 (1H, dd, *J* = 2.7, 8.1 Hz, Ar-H6), 6.46 (1H, d, *J* = 8.0 Hz, Ar-H2 & 6), 7.12 (1H, d, *J* = 8.5 Hz, Ar-H5), 7.34 (1H, d, *J* = 8.5 Hz, Ar-H3 & 5), 8.64 (1H, s, NH). MS (m/z): 453 (M^+), 455 (M^++2), 438 (base peak), 253, 243, 210, 200, 186, 109. Anal.(Calcd.) Found: C(47.69)47.66, H(3.78)3.77, N(6.18)6.16.

C.Antimicrobial Activity

The synthesized compounds (3a-3c & 4a-4c) were screened for antibacterial (*S. aureus, E. coli, P. aeruginosa*) and antifungal (*C. albicans, A. flavus, A. fumigatus*) activities by disk diffusion method at a concentration of 2 mg/mL using DMF as a solvent. The results were recorded in duplicate using Ciprofloxacin and Fluconazole as standards.

III. Results and Discussion

2-(4-bromo-3-methylphenoxy)acetate(1) was synthesized by the esterification of p-Bromo-m-cresol which is a phenol. The 2-(4-Bromo-3-methylphenoxy)acetohydrazide (2) was derived from Compound (1) by hydrazination reaction. The N-(substituted benzylidiene)-2-(4-bromo-3-methylphenoxy) acetamides (3a-c), which prepared from 2-(4-Bromo-3-methylphenoxy)acetohydrazide (2) via schiffs reaction, when cyclized with thioglycolic acid yielded potent antibacterial and antifungal 2-(4-bromo-3-methylphenoxy)-N-(4-oxo-2-arylthiazolidin-3-yl)acetamides(4a-c). The physical data of newly synthesized compounds 3a-c and 4a-c are presented in the Table I.

TABLE I
PHYSICAL DATA OF COMPOUNDS (3A-3C & 4A-4C)

Compd.	Molecular formula	Molecular weight	Yield (%)	m.p. (ºC)
3a	$C_{18}H_{20}N_3O_2Br$	390.27	72.03	195-196
3b	$C_{16}H_{14}N_2O_2BrCl$	381.65	65.55	215-216
3c	$C_{16}H_{15}N_2O_4Br$	379.20	60.38	222-223
4a	$C_{20}H_{22}N_3O_3BrS$	464.38	71.53	128-129
4b	$C_{18}H_{16}N_2O_3ClBrS$	455.76	65.32	126-127
4c	$C_{18}H_{17}N_2O_5BrS$	453.31	62.45	168-169

The synthetic procedure for conversion of compound 1, 2, 3a-c and 4a-c is suggested in Fig. 1.

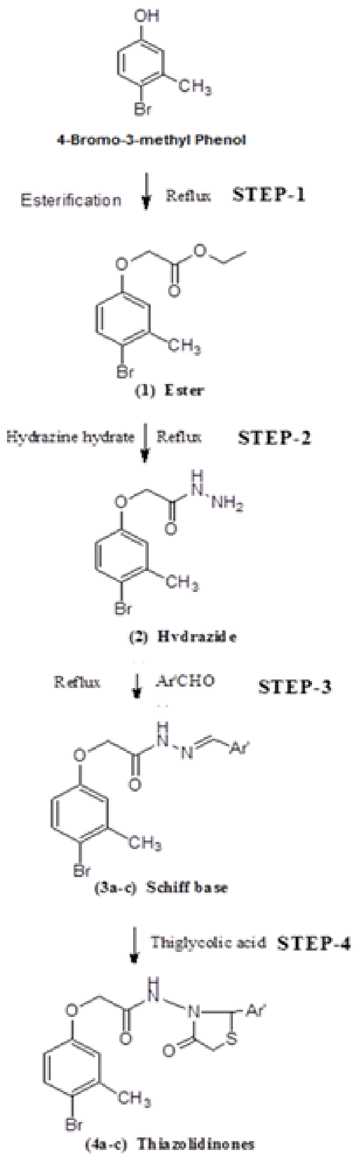

Fig. 1 Conversion of 4-bromo-3methyl phenol

The assigned structure, molecular formulae and the anomeric configuration of the newly synthesized compounds 3a-c and thiazolidinones 4a-c were further confirmed by and supported by mass, 1H-NMR, elemental analysis and IR spectral data, based on occurrence of molecular ion peak of the assigned structures, downfield shifting of protons and different stretching bands of the compounds. The newly synthesized compounds were further evaluated for their antimicrobial potential (Data given in Tables II & III)

TABLE II
ANTIBACTERIAL ACTIVITY OF COMPOUNDS (3A-3C & 4A-4C)

Compd.	Zone of Inhibition (mm)		
	S. aureus	*E. coli*	*P. aeruginosa*
3a	18.3 ± 0.33	19.3 ± 0.00	20 ± 0.00
3b	21.3 ± 0.33	22.3 ± 0.00	21.2 ± 0.00
3c	21 ± 0.00	22.2 ± 0.00	21.3 ± 0.33
4a	19.3 ± 0.00	19.3 ± 0.00	21.3 ± 0.33
4b	21.3 ± 0.67	23.3 ± 0.00	23.2 ± 0.00
4c	22.3 ± 0.00	21.5 ± 0.67	23.3 ± 0.33
Ciprofloxacin	27 ± 0.00	28 ± 0.00	27 ± 0.00
DMF	-	-	-

* All the values are expressed as mean ± SEM of triplicates

TABLE III
ANTIFUNGAL ACTIVITY OF COMPOUNDS (3A-3C & 4A-4C)

Compd.	Zone of Inhibition (mm)		
	C. albicans	*A. fumigatus*	*A. flavus*
3a	10.3 ± 0.00	13± 0.00	12.2± 0.00
3b	12.3 ± 0.33	10.3± 0.00	8.3± 0.00
3c	13.2 ± 0.00	12.3± 0.00	10.2± 0.00
4a	12.3 ± 0.00	10.2± 0.00	14± 0.00
4b	12.3 ± 0.33	14.3± 0.00	14.2± 0.00
4c	13.3 ± 0.00	12.3± 0.00	10± 0.00
Fluconazole	17 ± 0.00	23± 0.00	22± 0.00
DMF	-	-	-

* All the values are expressed as mean ± SEM of triplicates

IV. CONCLUSION

After carrying out the antimicrobial studies of newly synthesized compounds, it was found that each compound 3a-c and 4a-c possesses antibacterial and antifungal activities to certain extent. Among the newly synthesized derivatives, compound 4c was found to be most effective against *Staphylococcus aureus, Pseudomonas aeruginosa* and *Candida albicans* while compound 4b was found to be most effective against *Escherichia coli, Asperigillus flavus and Asperigillus fumigatus.* Some of the tested compounds: 3b, 3c, and 4a, have shown good antibacterial and antifungal activity whereas, the remaining compounds have shown moderate activity on the tested organisms. After comparing the antimicrobial results of newly synthesized compounds 3a-c and 4a-c, it was concluded that incorporation of thiazolidinone moiety in the aryloxy derivatives potentiates their antimicrobial activity.

REFERENCES

[1] G. Küçükgüze, A. Kocatepe, E. De Clercq, F. Sahin, and M. Güllüce, "Synthesis and biological activity of 4-thiazolidinones,

thiosemicarbazides derived from diflunisalhydrazide", Eur. J. Med. Chem., Vol. 41, pp. 353-359, 2006.
[2] N. K. Fuloria, V. Singh, M. Shaharyar, and M. Ali, "Synthesis, characterization and biological studies of new schiff bases and azetidinones derived from propionic acid derivatives", Asian J. Chem., vol. 20, pp. 6457-6462, 2008.
[3] N. K. Fuloria, V. Singh, M. Shaharyar, and M. Ali, "Synthesis, characterization and biological studies of novel imines and azetidinones derivatives of haloaryloxy moiety", Asian J. Chem., vol. 20, pp. 4891-4900, 2008.
[4] G. Küçükgüze, E. E. Oruç, S. Rollas, F. Sahin, and A. Ozbek, "Synthesis, characterization and biological activity of novel 4-thiazolidinones, 1,3,4-oxadiazoles and some related compounds", Eur. J. Med. Chem., vol. 37, pp. 197-206, 2002.
[5] P. Vicini, A.Geronikaki, K. Anastasia, M. Incerti, and F. Zani, "Synthesis and antimicrobial activity of novel 2-thiazolylimino-5-arylidene-4-thiazolidinones", Bioorg. Med. Chem., vol. 14: 3859-3864, 2006.
[6] V. G. C. S. Kandapalli, and S. R. Vajja, "Solvent free microwave accelerated synthesis of heterocyclic thiazolidine-4-ones as antimicrobial and antifungal agents", Bull. Kor. Chem. Soc., Vol. 35, pp. 1219-1222, 2010.
[7] B. M.Gurupadyya,M.Gopal, B.Padmashali, and Y. N. Manohara, "Synthesis and pharmacological evaluation of azetidin-2-ones and thiazolidin-4-ones encompassing benzothiazole", Ind. J. Pharm. Sci., Vol. 70, pp. 572-577, 2008.
[8] D. Visagaperumal, K. Jaya, R. Vijayaraj, and N. Anbalgan, "Microwave-induced synthesis of some new 3-substituted-1, 3-thiazolidin-4-ones for their potent antimicrobial and antitubercular activities", Int. J. ChemTech Res., Vo. 1, pp. 1048-1051, 2009.
[9] M. Ketan, and K. R. Desai, "Microwave assisted rapid and efficient synthesis of nitrogen and sulfur containing heterocyclic compounds and their pharmacological evaluation", Ind. J. Chem., 45(B): 1762-1766, 2006.
[10] B. P. Sharanabasppa, and M. G. Naganna, , " Synthesis of 3- (1 – benzyl – 1H - benzo [d] imidazol – 2 - l amino) – 2 - (3 – aryl - 1- phenyl – 1H - pyrazol - 4 - yl) thiazolidin - 4- ones and their antimicrobial activities", Int. J. Pharm. Sci. Res., Vol. 1, pp. 50-60, 2010.
[11] C. Milan, M. Maja, and D. Nela, "Design and synthesis of some thiazolidin-4-ones based on (7-Hydroxy-2-oxo-2H-chromen-4-yl) acetic acid", Molecule, Vol. 14, pp. 2501-2513, 2009.
[12] M. Parmeshwaran, and S. Gopalkrishnan, "Synthesis of coumarin heterocyclic derivatives with antioxidant activity and in vitro cytotoxic activity against tumour cells", Acta Pharm., 59: 159-170, 2009.
[13] D. Rajiv, S. K. Sonwane, S. K. Srivastava, and S. D. Srivastava, "Conventional and greener approach for the synthesis of some novel substituted-4-oxothiazolidine and their 5-arylidene derivatives of 2-methyl-benzimidazole: antimicrobial activities", J Chem. Pharm. Res., Vol. 2, pp. 415-423, 2010.
[14] A. Jigisha, A. Maroliwal, and K. C. Patel, "A novel microwave mediated synthesis of thiazolidinones derived from 1,2,4-triazoles over ZnCl2\DMF and evaluation of antimicrobial activity", J. Chem. and Pharm. Res., Vol. 2, pp. 392-404, 2010.
[15] N. Singh, , U. S. Sharma, N. Sutar, S. Kumar, and U. K. Sharma, "Synthesis and antimicrobial activity of some novel 2-amino thiazole derivatives", J Chem. and Pharm. Res., 2: 691-698, 2010.
[16] E. C. Taylor, H. Patel, and H. Kumar, "Synthesis of pyrazolo 3,4-*d*-pyrimidine analogues of the potent agent N-4-2-2-amino-4-3*H*-oxo-7*H*-pyrrolo 2,3-*d*-pyrimidin-5-yl ethyl benzoyl-*L*-glutamic acid (LY231514)", Tetrahedron, 48: 8089-8100, 1992.
[17] R. Gupta, N. K. Fuloria, and S. Fuloria, "Synthesis and antimicrobial activity evaluation of some schiff bases derived from 2-aminothiazole derivatives", Indon. J. Pharm., Vo. 24, pp. 35-39, 2013.
[18] R. Govindarajan,H. J. Jameela, andA. R. Bhat, "Synthesis of azetidinone and thiazolidinone derivatives of pyrazinoic acid for possible anti-tubercular, anti-fungal, anti-bacterial activity", Ind.J.Heterocycl.Chem.,Vol. 12, pp. 229-232, 2003.
[19] B. S. Vashi, D. S. Mehta, and V. H. Shah, "Synthesis and biological activity of 4-thiazolidinones, 2-azetidinones, 4-imidazolinone derivatives having thymol moiety", Ind. J. Chem., Vol.34B, pp. 802, 1995.
[20] H.B. Oza, & N. J. Datta, "Synthesis of new 1,2,4-triazolo-thiadiazoles and its 2-oxo azetidines as anti-microbial, anti-convulsant, anti-inflammatory agents", Ind. J. Heterocycl. Chem., Vol. 12, pp. 275-276, 2003.
[21] R. Gupta, N. K. Fuloria, and S. Fuloria, "Synthesis and antimicrobial profile newer heterocycles bearing thiazole moiety", South. Braz. J. Chem., Vo. 20, pp. 61-67, 2012.
[22] D.Patel, P. Kumari, andN. Patel, "Synthesis, characterization and biological evaluation of some thiazolidinone derivatives as antimicrobial agents, J. Chem.Pharm. Res., Vol. 2, pp. 84-91, 2010.
[23] N. K. Fuloria, V. Singh, M. Shaharyar, and M. Ali, "Synthesis, characterization and antimicrobial evaluation novel imines and thiazolidinones", Acta Pol. Pharm.- Drug Res., Vol. 66, pp. 141-146, 2009.