IJPSR (2018), Volume 9, Issue 2 **(Research Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 29 May, 2017; received in revised form, 27 October, 2017; accepted, 16 November, 2017; published 01 February, 2018

AN EFFICIENT, GREENER MICROWAVE ASSISTED MULTI-COMPONENT ONE POT SYNTHESIS OF [1, 3, 4] THIADIAZIN-2-YL-THIAZOLIDIN-4-ONES

Savita R. Dhongade* and Sandeep A. Kenawade

Research Laboratory in Heterocyclic Chemistry, Devchand College, Arjunnagar Kolhapur - 416012, Maharashtra, India.

Keywords:

[1,3,4]thiadiazin-2-ylamine, [1,3,4]thiadiazin-2-yl)-thiazolidin -4-one, PASS, Biological prediction study

Correspondence to Author:
Dr. Savita R. Dhongade

Associate Professor and Guide, Research Laboratory in Heterocyclic Chemistry, Devchand College, Arjunnagar, Kolhapur - 416 012, Maharashtra, India.

E-mail: savitadesai2010@gmail.com

ABSTRACT: This work involves synthesis of [1, 3, 4] thiadiazin-2-ylamine 3(a-c) derivatives from various substituted acetophenone derivatives 1(a-c), and thiosemicarbazide 2 mixed in ethanol and irradiation with microwaves which were directly used for next step. [1, 3, 4]Thiadiazin-2-yl)-thiazolidin-4-one 6(a-f) were synthesized in the second step from substituted-6H-[1, 3, 4] thiadiazin-2-ylamine 3(a-c), substituted aromatic aldehyde 4(a-b), and thioglycolic acid mixed in ethanol. After completion of the reaction products obtained 6(a-f) was confirmed by spectroscopy. Library of such [1, 3, 4] thiadiazin-2-ylamine and [1, 3, 4] thiadiazin-2-yl)-thiazolidin-4-one derivatives has been generated and the structures were subjected to PASS for their probabilities of being biologically active. Biological prediction study of the library was done to find out most active molecules. Computer programme PASS predicted for three activities with top probability for compound 3(a-c) as- 1. Mucomembranous protector, 2. Arylacetonitrilase inhibitor, 3. Macrophage elastase inhibitor. Similarly Compounds 6(a-f) were predicted for two activities with top probability as- 1. CC chemokine-4-receptor antagonist, 2. Phosphatase inhibitor.

INTRODUCTION: 1, 3, 4-thiadiazine derivatives involve in many biological processes and serve as medicinally interesting compounds [1, 2]. The wide range of therapeutic activities of 1, 3, 4-thiadiazine are antifungal [3], antibacterial [4], antimicrobial [5], anti-inflammatory [6] cardiovascular [7], anti-HIV [8], antidiabetic [9], antidepressant [10] *etc*. 4-Thiazolidinone derivatives have also been known to exhibit diverse bio-activities such as anti-convulsant [11], anti-diarrheal [12], anti-platelet activating factor [13], antihistaminic [14], anti-diabetic [15], Cyclooxygenase (COX) inhibitory [16], Ca^{2+}-channel blocker [17], platelet activating factor (PAF) antagonist [18], cardioprotective [19], anti-ischemic [20], anti-cancer [21], tumor necrosis factor-α antagonist [22] and nematicidal activities [23]. 2-Phenylimino-3-aryl-4- S- benzyl-6-tetra-O-acetyl-β-D-galactosylimino-2, 3-dihydro-1, 3, 5-thiadiazine (hydrochloride) derivatives [24] show antimicrobial activity against various pathogenic bacteria and fungi.

These biologically active spiroheterocycle inspired us to integrate thiadiazine moiety in a triazole framework [25]. Some new 1, 3, 4-thiadiazines with coumarin moieties and their derivatives [26] were shown to have antioxidant activity, employing different antioxidant assays (DPPH scavenging activity, iron chelating activity, power reducing activity).

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.9(2).650-55

Article can be accessed online on: www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.9(2).650-55

Again some new series of novel 3-(5-methyl-1-phenyl- 1H-1,2,3-triazol-4-yl)- 6-aryl- 7H- [1, 2, 4] triazolo[3,4b] [1,3,4] thiadiazine derivatives [27] shown antibacterial activity against four human pathogenic bacteria *viz. Escherichia coli, Klebseilla pneumoniae, Shigella dysentriae* and *Shigella flexnei*. Herein we report the synthesis of a new series of spiro-thiadiazines and their antimicrobial activity. The synthesis of heterocycles containing such multistructure in a molecule has received much attention in recent years [28].

PASS: PASS is a software application that predicts 565 possible biological activities of a user selected (set of) compound(s). These activities include 5-hydroxytryptamine antagonists, neuromuscular blocking agents, antibiotics, antidepressants, antiviral agents (AIDS), contraceptives, tumor necrosis factor antagonists and many others. Using PASS predictions, novel pharmaceutical agents have been discovered with anxiolytic, anti-inflammatory, antihypertensive, anticancer and other activities. PASS is applicable to chemical libraries containing millions of compounds.

The "the biological activity spectrum" is defined as the "intrinsic" property of a compound depending only on its structure and physico-chemical characteristics. Prediction of this spectrum by PASS is based on SAR analysis of the training set containing thousands of compounds which have many kinds of biological activities. In PASS biological activities are described qualitatively (“active” or “inactive”).

Importance of PASS:

1. Experimental determination of biological activity of a drug is time and cost consuming procedure, so making the use of PASS is generally important.
2. PASS can be effectively used for finding of compounds with required properties and without undesirable side effects.
3. It used for selecting the most prospective compounds from the set of available samples for specific screening.
4. For determining of more relevant screens for particular compound.

Due to this significance of PASS, it is used in the present study as a tool to design the drug with highest probable activity.

MATERIALS AND METHODS: All chemicals and solvents were reagent grade and used as purchased without any further purification. Analytical thin layer chromatography was performed on percolated silica gel 60-F 254 plates. IR spectra on KBr disks were recorded on a Schimazdu IR - 470 FT-IR spectrophotometer. The routine nuclear magnetic resonance spectra were taken in DMSO/$CDCl_3$ using a Bruker 300 MHz spectrophotometer with TMS as an internal standard. Chemical shift δ was given in ppm relative to TMS. The data found were in consistent with the proposed structure. Elemental analysis was done using EURO Vector Elemental Analyzer. Melting points are determined in an open capillary tube and are uncorrected.

Synthetic Procedure for the 5-phenyl-6H-[1, 3, 4] thiadiazin-2-ylamine 3(a): In 100 mL round bottom flask, acetophenone 1.20 g,(0.01 mole), and thiosemicarbazide 0.91 g, (0.01 mole) were mixed in ethanol (20 mL) and the reaction mixture was irradiated with microwaves at 20% microwave power (140 W) for 5 min. The completion of the reaction was confirmed by TLC (Ethyl acetate: Hexane 1:9). The reaction mixture was allowed to cool at room temperature, poured into crushed ice. The solid separated was filtered, washed with little ethanol and purified by recrystallization from ethanol to get pure products.

5-Phenyl-6H-[1, 3, 4] thiadiazin-2-ylamine 3(a):
Molecular Formula: $C_9H_9N_3S$,
Melting Point: 222 °C,

IR (KBr) ν_{max}: 1200 (C=S), 3318 (>NH) 3552 (-NH_2) cm^{-1}. H^1 NMR ($CDCl_3$, 300 MHz): δ 2.60 (s, 2H, CH_2), 6.94-7.36 (m, 5H, Ar-H), 9.45 (s, 2H, NH_2) ppm. ^{13}C NMR($CDCl_3$, 100 MHz): δ 21.09, 127.91, 129.90, 133.30, 140.00, 150.01, 154.91 ppm. Similarly derivatives 3b and 3c are synthesized.

5- (3-Nitro-phenyl)- 6H- [1, 3, 4] thiadiazin-2-ylamine 3(b):
Molecular Formula: $C_9H_8N_4O_2S$,
Melting Point: 206 °C,

IR (KBr) ν_{max}: 1330(C=S), 3010 (>NH), 3345 (-NH_2) cm^{-1}. H^1 NMR ($CDCl_3$, 300 MHz): δ 2.71 (s, 2H, CH_2), 7.66-8.99 (m, 4H, Ar-H), 9.78 (s, 2H, NH_2) ppm. ^{13}C NMR($CDCl_3$, 100 MHz): δ 21.18, 120.51, 126.41, 128.58, 132.28, 140.61, 142.27, 146.26, 150.55 ppm.

5-(4-Methoxy-phenyl)-6H- [1, 3, 4] thiadiazin-2-ylamine 3(c):
Molecular Formula: $C_{10}H_{11}N_3OS$,
Melting Point: 202 °C,

IR (KBr) ν_{max}: 1120 (C=S), 2965 (>NH), 3317 (-NH_2) cm^{-1}. H^1 NMR ($CDCl_3$, 300 MHz): δ 2.56 (s, 2H, CH_2), 3.87 (s, 3H, OCH_3), 6.90-7.98 (m, 4H, Ar-H), 9.67 (s, 2H, NH_2) ppm. ^{13}C NMR($CDCl_3$, 100 MHz): δ 18.09, 67.42, 121.97, 124.51, 127.55, 128.93, 124.12, 156.67 ppm. The products thus obtained 3(a-c) were directly used for next step.

Synthetic procedure for the 2-(2,4dichloro-phenyl)-3- (5-phenyl-6H- [1,3,4] thiadiazin-2-yl)-thiazolidin-4-one6(a-f): In a 100 mL round bottom flask, the product of step I *i.e.* 5-phenyl-6H-[1,3,4]thiadiazin-2-ylamine(3a) (0.001 mole), 2,4-dichlorob-enzaldehyde (0.001 mole), and thio glycolic acid (2-mercapto acetic acid) (0.001 mole) were mixed in ethanol (15 mL). The reaction mixture was irradiated with microwaves at 20% microwave power (140 W) for 4 mins. The completion of the reaction was confirmed by TLC (Ethyl acetate: Hexane 1:9). The reaction mixture was allowed to cool at room temperature and poured into crushed ice. The solid separated was filtered, washed with little ethanol and purified by recrystallization from ethanol to get pure product 6a.

2-(2, 4-Dichloro-phenyl)-3-(5-phenyl-6H-[1, 3, 4] thiadiazin-2-yl)-thiazolidin-4-one 6(a):
Molecular Formula: $C_{18}H_{13}Cl_2N_3OS_2$,
Melting Point: 228 °C,

IR (KBr) ν_{max}:750 (C–Cl), 1040 (C-N), 1750 (C=O), 3000 (Ar-CH), cm^{-1}. H^1 NMR (DMSO, 400 MHz): δ 2.49 (s, 2H, >CH_2), 3.26 (s, 2H, >CH_2), 6.06(s, 1H, >CH), 7.31-8.27(m, 8H, Ar-H), ppm. ^{13}C NMR(DMSO, 100 MHz): 21.29, 33.50, 67.50, 107.18, 117.95, 127.02, 128.07, 129.43, 130.58, 132.56, 132.87, 134.60, 135.07, 137.83, 152.18, 171.18 ppm. Similarly derivatives 6(b-f) are synthesized.

2- (4-Chloro-phenyl)- 3-(5-phenyl- 6H- [1, 3, 4] thiadiazin-2-yl)-thiazolidin-4-one6(b):
Molecular Formula: $C_{18}H_{14}ClN_3OS_2$,
Melting Point: 202 °C,

IR (KBr) ν_{max}:700 (C–Cl), 1040 (C-N), 1750 (C=O), 2950 (Ar-CH), cm^{-1}. H^1 NMR (DMSO, 400 MHz): δ 2.66 (s, 2H, >CH_2), 3.26 (s, 2H, >CH_2), 6.08 (s, 1H, >CH), 7.31-8.11(m, 9H, Ar-H), ppm. ^{13}C NMR(DMSO, 100 MHz): 21.00, 25.22, 71.50, 117.65, 127.02, 128.07, 129.63, 130.56, 132.50, 132.87, 134.60, 135.00, 137.89, 174.02 ppm.

2-(2, 4 Dichloro-phenyl)-3-[5-(3-nitro-phenyl)-6H-[1,3,4]thiadiazin-2-yl]-thiazolidin-4-one 6(c):
Molecular Formula: $C_{18}H_{12}Cl_2N_4O_3S_2$,
Melting Point: 210 °C,

IR (KBr) ν_{max}:700 (C–Cl), 1020 (C-N), 1355-1375 (N=O), 1740 (C=O), 2950 (Ar-CH), cm^{-1}. H^1 NMR ($CDCl_3$, 400 MHz): δ 2.50 (s, 2H, >CH_2), 3.55 (s, 2H, >CH_2), 5.97 (s, 1H, >CH), 7.11-8.04 (m, 7H, Ar-H), ppm. ^{13}C NMR($CDCl_3$, 100 MHz): 22.54, 29.48, 63.64, 114.81, 124.69, 130.65, 133.32, 136.62, 138.68, 141.81, 144.14, 145.44, 148.26, 149.59, 154.65, 161.33, 163.49, 180.08 ppm.

2-(4-Chloro-phenyl)-3-[5-(3-nitro-phenyl)-6H-[1, 3, 4]thiadiazin-2-yl]-thiazolidin-4-one6(d),
Molecular Formula: $C_{18}H_{13}ClN_4O_3S_2$,
Melting Point: 204 °C,

IR(KBr) ν_{max}:700 (C–Cl), 1020 (C-N), 1355-1375 (N=O), 1740 (C=O), 2950 (Ar-CH),cm^{-1}. H^1 NMR ($CDCl_3$, 400 MHz): δ 2.50 (s, 2H, >CH_2), 3.55 (s, 2H, >CH_2), 6.01 (s, 1H, >CH), 6.79-7.65 (m, 8H, Ar-H), ppm. ^{13}C NMR($CDCl_3$, 100 MHz): 21.08, 29.48, 67.48, 115.84, 118.84, 121.48, 124.69, 127.77, 130.65, 132.25, 135.21, 149.05, 153.03, 160.49, 161.33, 181.01 ppm.

2-(2,4Dichloro-phenyl)-3-[5-(4-methoxy-phenyl)-6H-[1,3,4]thiadiazin-2-yl]-thiazolidin-4-one6(e):
Molecular Formula: $C_{19}H_{15}Cl_2N_3O_2S_2$,
Melting Point: 212 °C,

IR (KBr) ν_{max}:700 (C–Cl), 1020 (C-N), 1300 (C-O), 1600 (C=C), 1740 (C=O), 2950 (Ar-CH), cm^{-1}. H^1 NMR ($CDCl_3$, 400 MHz): δ 2.38 (s, 2H, >CH_2), 3.22 (s, 2H, >CH_2), 3.92 (s, 3H, >OCH_3), 6.00 (s, 1H, >CH), 7.14-7.66 (m, 7H, Ar-H), ppm. ^{13}C NMR($CDCl_3$, 100 MHz): 21.17, 33.78, 55.10,

70.18, 107.11, 122.20, 126.88, 139.02, 140.07, 142.23, 143.38, 145.14, 145.87, 147.00, 147.77, 150.37, 179.89 ppm.

2-(4-Chloro-phenyl)-3-[5-(4 - methoxy - phenyl)-6H-[1, 3, 4]thiadiazin-2-yl]-thiazolidin-4-one6(f):
Molecular Formula: $C_{19}H_{16}ClN_3O_2S_2$,
Melting Point: 230 °C,

IR (KBr) ν_{max}:700 (C–Cl), 1020 (C-N), 1300 (C-O), 1600 (C=C), 1740 (C=O), 2950 (Ar-CH), cm^{-1}. H^1 NMR ($CDCl_3$, 400 MHz): δ 2.38 (s, 2H, $>CH_2$), 3.22 (s, 2H, $>CH_2$), 3.90 (s, 3H, $>OCH_3$), 6.01 (s, 1H, >CH), 7.20-7.60 (m, 8H, Ar-H), ppm. ^{13}C NMR($CDCl_3$, 100 MHz): 21.17, 33.78, 55.10, 70.18, 107.11, 122.20, 126.88, 139.02, 140.07, 142.23, 143.38, 145.87, 147.77, 150.37, 179.89 ppm.

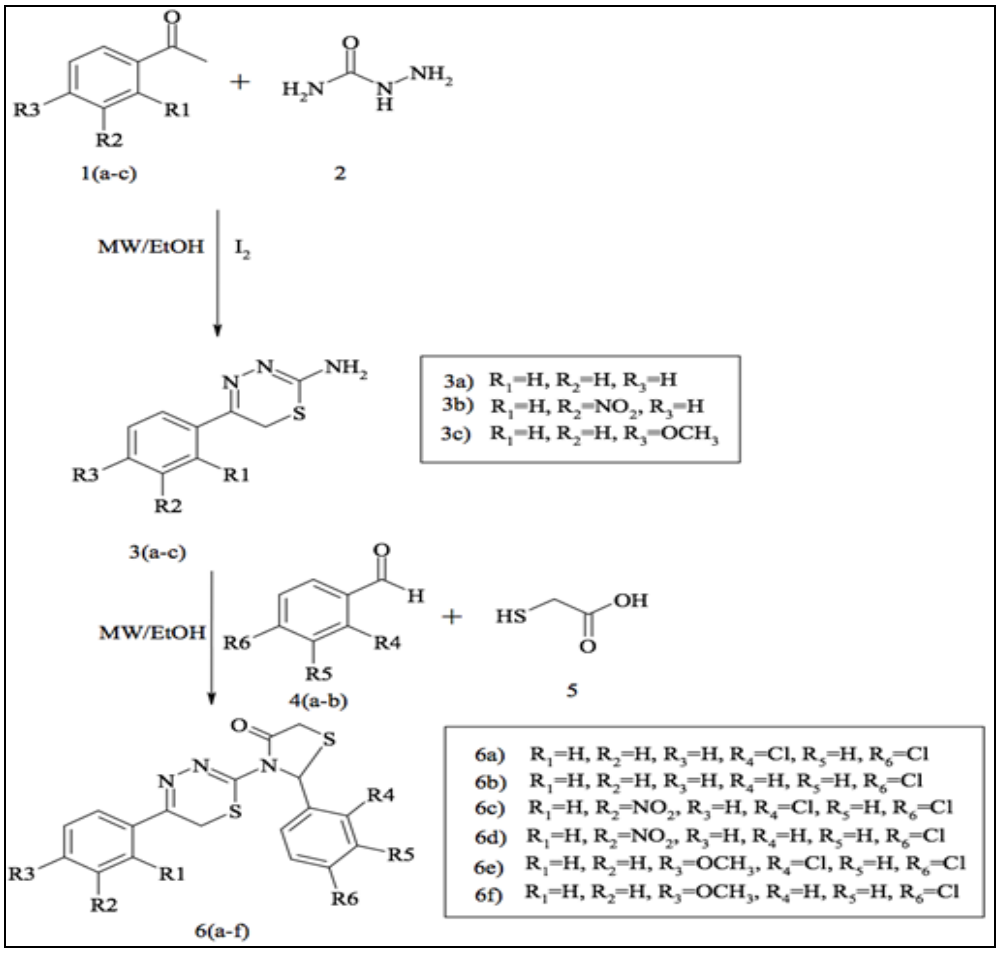

TABLE 1: ANALYTICAL DATA OF THE COMPOUNDS 3(a-c)

Product	Time (in min.)	Yield	M. P. °C	Mol. Formula	Found / (Calculated) %		
					C	H	N
3(a)	5	75	222	$C_9H_9N_3S$	56.51 (56.52)	4.65 (4.74)	21.37 (21.97)
3(b)	3	70	206	$C_9H_8N_4O_2S$	45.70 (45.76)	3.29 (3.41)	23.50 (23.71)
3(c)	4	72	202	$C_{10}H_{11}N_3OS$	54.20 (54.28)	4.99 (5.01)	18.60 (18.99)

TABLE 2: ANALYTICAL DATAOF THE COMPOUNDS 6(a-f)

Product	Time (in min.)	Yield	M. P. °C	Mol. Formula	Found / (Calculated) %		
					C	H	N
6(a)	4	55	228	$C_{18}H_{13}Cl_2N_3OS_2$	51.02 (51.19)	3.05 (3.10)	9.90 (9.95)
6(b)	5	60	202	$C_{18}H_{14}ClN_3OS_2$	55.60 (55.73)	3.61 (3.64)	10.70 (10.83)
6(c)	3	62	210	$C_{18}H_{12}Cl_2N_4O_3S_2$	46.20 (46.26)	2.50 (2.59)	11.90 (11.99)
6(d)	4	65	204	$C_{18}H_{13}ClN_4O_3S_2$	49.85 (49.94)	3.00 (3.03)	12.90 (12.94)
6(e)	4	60	212	$C_{19}H_{15}Cl_2N_3O_2S_2$	50.40 (50.45)	3.30 (3.34)	9.20 (9.29)
6(f)	4.5	68	230	$C_{19}H_{16}ClN_3O_2S_2$	54.55 (54.60)	3.63 (3.86)	10.01 (10.05)

RESULTS AND DISCUSSION: The confirmed structures were subjected to computer programme PASS for the prediction of their biological activities. Compound 3(a-c) were predicted for three activities with top probability.

- Mucomembranous protector
- Arylacetonitrilase inhibitor
- Macrophage elastase inhibitor

TABLE 3: BIOLOGICAL PREDICTION ANALYSIS OF ACTIVITIES OF DERIVATIVES 3(a-c)

Activity Comp	Muco-membranous protector	Arylacetonitrilase inhibitor	Macrophage elastase inhibitor
	Pa	Pa	Pa
3(a)	0.802	0.797	0.792
3(b)	0.726	0.794	0.729
3(c)	0.721	0.563	0.776

Compounds 6(a-f) were predicted for two activities with top probability.

1. CC chemokine 4 receptor antagonist
2. Phosphatase inhibitor

TABLE 4: BIOLOGICAL PREDICTION ANALYSIS OF ACTIVITIES OF DERIVATIVES 6(a-f)

Activity Comp	CC chemokine 4 receptor antagonist	Phosphatase inhibitor
	Pa	Pa
6(a)	**0.861**	0.762
6(b)	0.171	**0.774**
6(c)	0.800	0.721
6(d)	0.158	0.733
6(e)	0.804	0.733
6(f)	0.164	0.744

CONCLUSION: In summary, we have developed an efficient method for the synthesis of [1, 3, 4] thiadiazin-2-ylamine 3(a-c) and [1, 3, 4] thiadiazin-2-yl)- thiazolidin- 4- one 6(a-f) derivatives with excellent yield under microwave irradiation, which attains completion in 5 - 7 min in an organic medium and may provide a useful route for the rapid drug discovery. Biological prediction analysis revealed that the 2-(2, 4 dichloro-phenyl)-3-(5-phenyl-6H-[1, 3, 4] thiadiazin-2-yl)-thiazolidin-4-one6(a) is predicted to be moderately active as CC chemokine 4 receptor antagonist. 2-(4-chloro-phenyl)-3-(5-phenyl-6H-[1, 3, 4] thiadiazin-2-yl)-thiazolidin-4-one 6(b) can be most active in the series as phosphatase inhibitor and hence it is recommended for the screening of the same activity.

ACKNOWLEDGEMENT: The authors acknowledge UGC for providing financial assistance under the scheme of Major Research Project 41-305/2012 (SR) for availing research facilities in Research Laboratory in Heterocyclic Chemistry at Devchand College, Arjunnagar, Maharashtra, India.

CONFLICT OF INTEREST: Nil

REFERENCES:

1. Akberali PM: Ph.D. Thesis. Mangalore University 1991.
2. Stokes EJ and Ridgway GL: Clinical Bacteriology. London and New York Publisher & Distributors, Fifth Edition 1980.
3. Holla BS, Akberali PM and Shivananda MK: Farmaco. 2001; 56: 919-927.
4. Friedman MR, Toyne KJ, Goodby JW and Hird M: J. Mater. Chem. 2001: 2759-2772.
5. Walker GN and Smith RT: J. Org. Chem. 1971; 36: 305-308.
6. Sahin G, Palaska E, Kelicen P, Demirdamar R, Altinok G and Arzneim: Forsch, Drug Res. 2001; 51: 478-484.
7. Palaska E, Sahin G, Kelicen P, Durlu NT and Altinok G: Farmaco. 2002; 57: 101-107.
8. Mullican MD, Wilson MW, Connor DT, Kostlan CR, Schrier DJ and Dyer RD: J. Med. Chem. 1993; 36: 1090-1099.
9. Collins CH, Lyne PM, Grange JM, Falkinham JO and Collins: Lyne's Microbiological Methods, Butterworth, London 1970.
10. Mullen BG, Decory RT, Mitchell TJ, Allen DS, Kin solving Vassil CR and Georgiev B: J. Med. Chem. 1988; 31: 2008-2014.
11. Ragab FA, Eid NM and El-Tawab HA: Synthesis and anticonvulsant activity of new thiazolidinone and thioxoimidazolidinone derivatives derived from furochromones. Pharmazie 1997; 52: 926-929.
12. Mazzoni O, Bosco AM, Grieco P, Novellino E, Bertamino A, Borelli F, Capasso R and Diurno MV: Synthesis and pharmacological activity of 2-(substituted)-3-{2 [(4-phenyl-4-cyano) piperidino] ethyl}-1,3-thiazolidin-4-ones.Chem. Biol. Drug Design 2006; 67: 432-436.

13. Tanabe Y, Okumura H, Nagaosa M and Murakami M: Highly stereo selective synthesis of the antiplatelet activating factor, 4-thiazolidinones, using silyl derivatives of 2-mercaptoalkanoic acids. Bull. Chem. Soc. Jpn. 1995; 68: 1467-1472.
14. Tindara P, Maria B, Maria GV, Giovanna F, Francesco O, Clara C and Rita CP: 3, 3′-Di [1, 3-thiazolidine-4-one] system. II. Anti-inflammatory and anti-histaminic properties in new substituted derivatives. Eur. J. Med. Chem. 1987; 22: 67-74.
15. Prabhakar V and Vipan K: Synthesis and antidiabetic activity of N'-[3-(alkyl/aryl substituted)-4-oxo-1, 3 thiazolidin-2-yeidene]-2-(pyrazin-yloxy) acetohydrazide. Acta Pharmaceutica Sciencia 2010; 52: 411-415.
16. Taranalli AD, Bhat AR, Srinivas S and Saravanan E: Anti-inflammatory, analgesic and antipyretic activity of certain thiazolidinones. Indian J. Pharm. Sci. 2008; 70: 159-164.
17. Verma A and Saraf SK: 4-Thiazolidinone –A biologically active scaffold. Eur. J. Med. Chem. 2008; 43: 897-905.
18. Rollas S and Kucukguzel SG: Biological activities of hydrazone derivatives. Molecules 2007; 12: 1910-1939.
19. Kato T, Ozaki T, Tamura K, Suzuki Y, Akima M and Ohi N: Novel calcium antagonists with both calcium overload inhibition and antioxidant activity, Structure-activity relationships of thiazolidinone derivatives. J. Med. Chem. 1999; 42: 3134-3146.
20. Raghubir R, Verma R, Samuel SS, Raza S, Haq W and Katti SB: Anti-stroke profile of thiazolidin-4-one derivatives in focal cerebral ischemia model in rat. Chem. Biol. Drug Design 2011; 78: 445-453.
21. Danylo K, Dmytro K, Olexandr V, Lucjusz Z and Roman L: A facile synthesis and anticancer activity evaluation of spiro[thiazolidinone-isatin]conjugates. Sci. Pharm. 2011; 79: 763-777.
22. Mosula L, Zimenkovsky B, Havrylyuk D, Missir AV, Chirita IC and Lesyk R: Synthesis and antitumor activity of novel 2-thioxo-4-thiazolidinones with benzothiazole moieties. Farmacia. 2009; 57: 321-330.
23. Srinivas A, Nagaraj A and Reddy CS: Synthesis and biological evaluation of novel methylenebisthiazolidinone derivatives as potential nematicidal agents. J. Heterocycl. Chem. 2008; 45: 999-1003.
24. Mahalle PR: Der Pharma Chemica. 2017; 9(10): 120-122.
25. Dabholkar VV, Naik P, Karekar A and Shinde N: Der Pharma Chemica. 2014; 6(6): 108-113.
26. Cacic M, Pavic V, Molnar M, Sarkanj B, and Has-Schon E: Molecules 2014: 19: 1163-1177.
27. Ravi G, Ravindernath A, Nagaraj A, Damodhar S and Nageshwara Rao G: Der Pharma Chemica. 2014; 6(4): 223-232.
28. Srinivas A, Nagaraj A and Reddy CS: Synthesis and *in vitro* study of methylene-bistetrahydro[1,3]thiazolo[4,5-c]isoxazoles as potential nematicidal agents. Eur. J. Med. Chem. 2010; 45: 2353-2358.

How to cite this article:
Dhongade SR and Kenawade SA: An efficient, greener microwave assisted multi-component one pot synthesis of [1, 3, 4] thiadiazin-2-yl-thiazolidin-4-ones. Int J Pharm Sci & Res 2018; 9(2): 650-55. doi: 10.13040/IJPSR.0975-8232.9(2).650-55.