TABLE 2: ANTIHIV AND ANTIYFV ACTIVITIES OF TITLE COMPOUNDS

Compound	AntiHIV activity (μM)			AntiYFV activity (μM)	
	EC_{50}	CC_{50}	%Protection	EC_{50}	CC_{50}
S1	NT	NT	-	>100	100
S2	NT	NT	-	>100	100
S3	>104	104	43.68	2.5	>100
S4	>154	154	21.38	>20	20
S5	>132	132	24.20	>20	20
S6	>52.0	52.0	16.32	>20	20
S7	>98.8	98.8	15.87	15	>100
S8	>16.7	16.7	16.29	>4	4

EC_{50} refers to the effective concentration in 50% population and CC_{50} refers to the cytotoxic concentration in 50% population and NT indicates not tested.

topathic effect are presented in Table 2. Among the compounds tested, two compounds S3 and S7 showed promising activity with EC_{50} of 2.5 μM and 15 μM, respectively, CC_{50} of >100 μM and selectivity index of >40 and >6.6 respectively. These compounds were more potent than ribavirin (EC_{50}=49 μM and CC_{50} =>100 μM). From these results, compound 1-(4'-chlorobezylidene) amino-3-hydroxy guanidine (S3) emerged as a potent compound with both antiHIV and antiYFV activities.

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Microwave-Assisted Synthesis, and AntiHIV Activity of 2,3-Diaryl-1,3-Thiazolidin-4-Ones

D. SRIRAM*, P. YOGEESWARI AND T. G. ASHOK KUMAR
Medicinal Chemistry Research Laboratory, Pharmacy Group,
Birla Institute of Technology and Science, Pilani-333 031

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Several 1,3-thaizolidin-4-ones bearing variously substituted diaryl ring at C-2 and N-3 positions have been synthesized utilizing microwave irradiation and evaluated for their antiHIV and antiYFV activities. The results of the *in vitro* antiHIV evaluation showed that compound DS13 proved to be

***For correspondence**
E-mail: dsriram@bits-pilani.ac.in

an effective inhibitor of HIV-1 replication with EC_{50} of 10 μM, CC_{50} of 120 μM and percentage protection of 104%.

Reverse transcriptase (RT) is a key enzyme, which plays an essential and multifunctional role in the replication of the human immunodeficiency virus type-1 (HIV-1) and thus constitutes an attractive target for the development of new drugs useful in AIDS therapy[1]. Two classes of compounds, nucleoside and non-nucleoside RT inhibitors potently and selectively inhibit this enzyme and play a key role in the combination therapy for HIV infections. Recently 2,3-diaryl-1,3-thiazolidin-4-one derivatives have documented to be highly effective in inhibiting HIV-1 replication at nanomolar concentrations acting as RT inhibitors[2-4]. From the structure-activity relationship (SAR) point of view, the antiHIV activity was strongly dependent on the nature of the substituents at C-2 and N-3 positions of the thiazolidinone ring. Starting from these findings as leads, to shed more light on the SAR of this class of compounds, in the present paper we report herein the synthesis of an extensive set of 2,3-diaryl-1,3-thiazolidin-4-ones bearing various substituents at various positions of the aryl ring especially at C-2 and N-3 and evaluated their antiHIV activity.

Melting points were determined in one end open capillary tubes on a Buchi 530 melting point apparatus and are uncorrected. Infrared (IR) and proton nuclear magnetic resonance (^{1}H-NMR) spectra were recorded for the compounds on a Jasco IR Report 100 (KBr) and a Brucker Avance 300 MHz instrument, respectively. Chemical shifts are reported in parts per million (ppm) using tetramethylsilane (TMS) as an internal standard. All exchangeable protons were confirmed by addition of D_2O. Elemental analysis (C, H, N) was carried out on a Perkin Elmer Model 240C analyser.

To a stirred solution of aromatic amine (0.01 mol) in dry toluene (50 ml), 2-mercapto acetic acid (0.02 mol) and the appropriate aromatic aldehydes (0.01 mol) were added and irradiated in an unmodified domestic microwave oven at power setting of 80% with 30 seconds/cycle (Make: LG, input: 220 V~50Hz, 980 W, 4.7°A and frequency: 2450 MHz). The number of cycle in turn depended on the completion of the reaction, which was checked by thin layer chromatography (TLC) considering all the reactants in the analysis. The reaction timing varied from 6 to 8 min. The solution obtained after the completion of the reaction was kept at 0° for 30 min. During this time the excess of unreacted mercapto acetic acid was freezed out at the bottom and the clear solution was decanted. After removal of the solvent under reduced pressure, the oily residue was treated with a mixture of ethanol and diethyl ether in the ratio 6:4 to yield solid titled compounds in the yields ranging from 64-82%. Physical and spectral data of representative compounds are as follows.

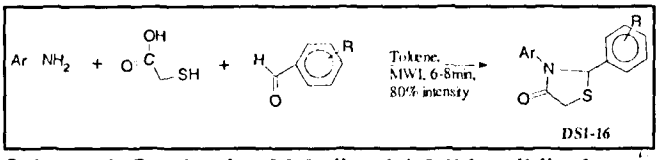
DS1, mp: 104°, yield: 68%; ^{1}H-NMR δ ppm (DMSO d_6): 3.87 (dd, 1H, J=15.7 Hz, 5-H_A), 4.09 (dd, 1H, J=1.4 Hz, 5-H_B), 7.06-7.25 (m, 9H, ArH and H-2). Anal- ($C_{15}H_{11}NOSClF$) C, H, N. DS6, mp: 95°, yield: 79%, ^{1}H-NMR δ ppm (DMSO d_6): 1.1 (s, 6H, CH3), 3.86 (dd, 1H, J=15.1 Hz, 5-H_A), 4.11 (dd, 1H, J=1.9 Hz, 5-H_B), 7.10-7.36 (m, 8H, ArH and H-2). Anal. ($C_{17}H_{16}N_2O_3S$) C, H, N. DS8, mp: 121°, yield: 70%, ^{1}H-NMR δ ppm (DMSO d_6): 2.1 (s, 3H, CH_3), 3.86 (dd, 1H, J=15.7 Hz, 5-H_A), 4.18 (dd, 1H, J=1.5 Hz, 5-H_B), 7.06-7.46 (m, 8H, ArH and H-2). Anal. ($C_{16}H_{13}NOSCl_2$) C, H, N. DS13, mp: 100°, yield: 64%; ^{1}H-NMR δ ppm (DMSO d_6): 3.84 (dd, 1H, J=15.1 Hz, 5-H_A), 4.22 (dd, 1H, J=1.9 Hz, 5-H_B), 6.86 (s, 1H, H-2), 7.12-7.55 (m, 4H, ArH of 2-chlorophenyl), 7.60-8.20 (m, 4H, ArH of 2-pyridyl). Anal. ($C_{14}H_{11}N_2OSCl$) C, H, N. DS15, mp: 184°, yield: 65%, ^{1}H-NMR δ ppm (DMSO d_6): 2.25 (s, 3H, CH_3), 3.92 (dd, 1H, J=15.4 Hz, 5-H_A), 4.13 (dd, 1H, J= 1.9 Hz, 5-H_B), 7.05-8.25 (m, 8H, ArH and H-2). Anal. ($C_{15}H_{13}N_2OSCl$) C, H, N.

Candidate agents were dissolved in dimethylsulfoxide, and then diluted 1:100 in cell culture medium before preparing serial half-log10 dilutions. T4 lymphocytes (CEM cell line) were added and after a brief interval HIV-1 was added, resulting in a 1:200 final dilution of the compound. Uninfected cells with the compound served as a toxicity control, and infected and uninfected cells without the compound served as basic controls. Cultures were incubated at 37° in a 5% carbon dioxide atmosphere for 6 days. The tetrazolium salt, XTT was added to all the wells, and cultures were incubated to allow formazan color development by viable cells. Individual wells were analyzed spectrophotometrically to quantitative formazan production, and in addition were viewed microscopically for detection of viable cells and confirmation of protective activity[5].

The synthesis of the 2,3-diaryl-1,3-thiazolidin-4-ones (DS1-15) was accomplished by reacting substituted benzaldehyde with an equimolar amount of an appropriate substituted aromatic amine in the presence of an excess of mercapto acetic acid in toluene utilizing microwave irradiation (Scheme 1). Unlike the conventional methods[3,4]

TABLE 1: PHYSICAL CONSTANTS OF 2,3-DIARYL-1,3-THIAZOLIDIN-4-ONES

Compound	Ar	R	Elemental analysis Found (Calculated)			mp °	Yield (%)
			C	H	N		
DS1	4-F-C_6H_4-	4-Cl	58.67 (58.54)	3.61 (3.60)	4.57 (4.55)	104	68
DS2	4-F-C_6H_4-	2-Cl	58.63 (58.54)	3.58 (3.60)	4.52 (4.55)	84	72
DS3	4-F-C_6H_4-	3-NO_2	56.72 (56.60)	3.46 (3.48)	8.74 (8.80)	147	65
DS4	4-F-C_6H_4-	4-N(CH_3)2	64.38 (64.53)	5.36 (5.41)	8.81 (8.85)	124	82
DS5	4-F-C_6H_4-	2-OH	62.31 (62.27)	4.10 (4.18)	4.77 (4.84)	53	82
DS6	2,6-(CH_3)2-C_6H_3-	4-NO2	62.21 (62.18)	4.97 (4.91)	8.62 (8.53)	95	79
DS7	2,6-(CH_3)2-C_6H_3-	4-OH	68.25 (68.20)	5.77 (5.72)	4.67 (4.68)	195	74
DS8	3-Cl, 2-CH_3-C_6H_3-	4-Cl	56.87 (56.81)	3.86 (3.87)	4.11 (4.14)	121	70
DS9	3-Cl, 2-CH_3-C_6H_3-	2-Cl	56.90 (56.81)	3.95 (3.87)	4.23 (4.14)	75	69
DS10	3-Cl, 2-CH_3-C_6H_3-	4-N(CH_3)$_2$	62.45 (62.33)	5.62 (5.52)	8.14 (8.08)	75	79
DS11	3-Cl, 2-CH_3-C_6H_3-	2-OH	60.12 (60.09)	4.52 (4.41)	4.45 (4.38)	93	81
DS12	2,6-(Cl)2-C_6H_3-	4-NO_2	48.96 (48.80)	2.82 (2.73)	7.68 (7.59)	73	78
DS13	2-C_5H_4N-	2-Cl	57.99 (57.83)	3.90 (3.81)	9.65 (9.63)	100	64
DS14	2-C_5H_4N-	4-Cl	58.09 (57.83)	3.86 (3.81)	9.60 (9.63)	88	68
S15	3-CH_3-2-C_5H_4N-	4-Cl	59.22 (59.11)	4.32 (4.29)	9.21 (9.19)	184	65



Scheme 1: Synthesis of 2,3-diaryl-1,3-thiazolidin-4-ones

(reaction time 48 h and yields of 30-70%), microwave-assisted reactions were very facile (6-8 min) and provided very good yields (64-82%, Table1). Purity of the compounds was checked by TLC and elemental analyses. Both analytical and spectral data (^{1}H-NMR) of all the synthesized compounds were in full agreement with the proposed structures.

Some of the compounds were tested for antiHIV activity by determining their ability to inhibit the replication of HIV-1 in CEM cell line. As shown in Table 2, compound DS13 inhibited the HIV-1 replication with EC_{50} of 10.1 μM, CC_{50} of 120 μM and maximum protection of 104%. Other compounds did not show marked antiHIV activity at a concentration significantly below their toxicity threshold. These results indicated that the presence of halogen at C-2 and C-6 positions on phenyl ring and the presence of 2-pyridyl

TABLE 2: ANTIHIV ACTIVITY OF 2,3-DIARYL-1,3-THIAZOLIDIN-4-ONES

Compound	AntiHIV screening (μM)		
	EC_{50}	CC_{50}	% Protection
DS1	>74.8	74.8	14.36
DS2	>3.84	3.84	15.14
DS4	>3.63	3.63	18.65
DS5	>5.22	5.22	16.91
DS7	>47.4	47.4	30.01
DS8	>7.44	7.44	13.31
DS9	>51.0	51.0	26.14
DS10	>200	>200	21.40
DS11	>119	119	20.22
DS12	>12.1	12.1	14.75
DS13	10.1	120	104
DS15	>200	>200	12.50

EC_{50} refers to the effective concentration in 50% population and CC_{50} refers to the cytotoxic concentration in 50% population and NT indicates not tested.

substitutent at N-3 position of thiazolidinone ring were important requirements for antiHIV activity.

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Antiinflammatory activities of *Calamus rotang* Mill

G. SENTHILVEL*, A. ANOOP, M. JEGADEESAN[1], P. THIRUGNANASAMBANTHAM AND E. MAYISVREN

Rumi Herbals, B 25, Kambar Salai, Mugappair West, Chennai-600 037

[1]Department of Siddha Medicine, Faculty of Sciences, Tamil University, Thanjavur-613 007.

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***Calamus rotang* is a shrub, which is not much explored scientifically. Studies on the ethanolic (95%) extract of rhizome exhibited antiinflammatory activity in carrageenan-induced paw oedema and cotton pellet granuloma pouch models and the results were comparable with that of standard drug Phenylbutazone.**

Calamus rotang Linn (Family: Palmae) is a shrub, distributed endemically in India[1]. Rhizomes are astringent, acrid and bitter in taste. They are used as expectorant, antiinflammatory, diuretic, febrifuge and as tonic[2]. This plant has been traditionally used for reducing inflammation; hence, 95% ethanol extract of *C. rotang* (CRE) was evaluated for antiinflammatory activity in different phases of inflammation in animal models.

Rhizomes were collected from Coutrallam, Tamilnadu and authenticity was confirmed with local Floras. They were shade dried, cut into small pieces and powdered in a pulverizer. Coarse powder was extracted with ethanol using Soxhlet apparatus. CRE was suspended in 0.75% carboxy methyl cellulose and used throughout the experiment. They were analysed for antiinflammatory activity by carrageenan-induced paw oedema and cotton pellet granuloma models.

***For correspondence**

E-mail: anoopaustin@rediffmail.com

Male Wistar rats weighing between 150 and 200 g procured from King Institute, Guindy, Chennai were selected for the studies. The study was carried in accordance with the rules and regulations laid down by the Institutional Animal Ethical Committee.

For carrageenan-induced paw oedema model, rats were grouped into 7 groups, containing 6 animals per group. Group 1 served as negative control (1 ml of saline). The second group served as positive control (phenylbutazone 5 mg/kg), while the other groups received CRE in different doses of 50, 100, 150, 200 and 250 mg/kg orally. Oedema was induced as per standard methods[3]. The paw volume was measured 0 h and 3 h, after the injection of carrageenan (0.1 ml 1% w/v). Drug pretreatment was given 1 h before the injection of carrageenan. Percent inhibition of oedema was calculated[4].

In cotton pellet granuloma model, rats were divided into 7 groups, containing 6 animals per group. Group 1 served