ORIGINAL RESEARCH ARTICLES

SYNTHESIS AND BIOLOGICAL ACTIVITY OF 2-(4-SUBSTITUTED BENZYLIDENE)-7-METHYL-2*H*-THIAZOLO[3, 2-*a*] PYRIMIDINE-3,5-DIONES

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ABSTRACT

The organosulphur thiazolo-pyrimidines are fused heterocyclic compounds that can be anticipated as 7-thio counterparts of the genuine purine bases such as guanine and adenine. They have attained a growing significance in the domain of drug chemistry because of their diverse pharmacological activities. In the current study, 2-substituted benzylidene-7-methyl-2*H*-thiazolo [3,2-a] pyrimidine-3,5-dione derivatives were synthesised. The synthetic compounds were tested against the human myelomonocytic leukaemia cell line (U-937) for their ability to inhibit cancer cell growth as well as against Gram negative *E. coli* (MTCC 40) and Gram positive *S. aureus* (MTCC 87) for their ability to inhibit bacterial growth. The amine and halogen containing compounds exhibited the strongest anticancer and antibacterial effects among all the derivatives in series (7a-j). Compounds 7h, 7e, 7a, 7b, 7c, 7i, and 7j displayed improved activity in both assays compared to standard andriyamycin and ciprofloxacin, whereas 7d, 7f, and 7g were shown to be moderately active. Through the use of IR, NMR and mass spectrum analyses, the molecular structures of the synthesized compounds were determined.

Keywords: Thiazolo-pyrimidines, antibacterial, thiopurine bases, anticancer

INTRODUCTION

The World Health Organization (WHO) estimated that in 2030, there will be more than 10 million deaths worldwide from cancer, making it one of the deadliest diseases in the medical field[1]. The marketed chemotherapeutic agents feature several constraints such as complex synthesis and isolation procedures, high systemic toxicity and drug resistance. Therefore, there is a high interest in the advancement of anticancer agents[2]. Heterocyclic compounds possessing a pyrimidine nucleus have found extended relevance in the pharmacological areas such as anti-viral, anti-HIV, anti-bacterial and especially as an anticancer. Hoff *et al.* reported thienopyrimidine as a novel and patented small molecule scaffold for promising antitumor agents[3]. Presently, fused derivatives have fascinated diverse researchers, due to their synergistic effect on biological activities[4]. In addition, reports on numerous fused pyrimidine analogues such as tyrosine kinase and cyclin-dependent kinase inhibitors, mediators of mitogenic signals and a variety of additional cell functions, such as migration, proliferation, differentiation, metabolism, and immune responses, have been published recently. Furthermore, it has been noted that some of these compounds may prevent the proliferation of different cancer cell lines[5]. The versatile biological activities like antimicrobial[6, 7], antioxidant[8, 9], anticonvulsant[10], anti-inflammatory[11], antinociceptive[12], analgesic[13], antiparkinsonian[14], antiviral[15] and antibiofilm properties[16] of fused pyrimidinones have qualified them as scaffolds with conceivable medicinal properties seeking significant attention from both synthetic and medicinal chemists. These substances also happened to be effective as 5-HT_2 receptor antagonists[17] and inhibitors of xanthineoxidase[18], CDC25B phosphatase enzymes[19], and the Bcl-2 family of proteins[20]. Thiazole and pyrimidine moieties are the active pharmacophores of various bioactive molecules. Thus, the annulations of a pyrimidine ring on the biologically diverse thiazolo moiety results in an attractive heterocyclic scaffold to be utilized for exploiting chemical diversity. The thiazolo-pyrimidines

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can be regarded as 7-thio counterparts of the genuine purine bases such as guanine and adenine[21]. Hence, here an attempt is made to synthesize 2-substituted benzylidene-7-methyl-2*H*-thiazolo[3,2-*a*]pyrimidine-3,5-dione derivatives and evaluate their anticancer and antimicrobial potential.

EXPERIMENTAL STUDIES

Chemical and reagents

The synthesis was carried out using chemicals of LR grade and procured from Spectrochem Pvt. Ltd., Sigma-Aldrich Chemicals Pvt. Ltd., Merck India and Loba Chemie. All the solvents used in the reactions were of LR grade and purified before use. To track the reaction, pre-coated plates (Merck 60F254) were used for thin layer chromatography (TLC). Several solvent systems, including cyclohexane: ethylacetate (6:4 V/V) and petroleum ether: ethylacetate: methanol (6:3:1), were utilized to create chromatograms.

Instrumentation

Melting point, IR, 1H NMR and mass spectroscopy were used to identify and characterize the compounds. Melting points were calculated using the capillary method with a melting point instrument (Perfit India) and are uncorrected. The Bruker -E FTIR-ATR spectrometer was used to record all the infrared (IR) spectra. The 1H NMR spectra were captured on Bruker Avance 2400 (400MHz) spectrometer at SAIF, Punjab University, Chandigarh, and JEOL JNM-ECS400 (400MHz) spectrometer at Indian Institute of Technology (IIT), Mumbai, using DMSO or $CDCl_3$ as solvents. At SAIF, Punjab University, Chandigarh, mass spectra were captured utilising an EIMS-based approach on a Micromas Q-T micro spectrometer.

Synthesis of 2-thio-6-methyluracil (3)

A 500 mL flask was filled with thiourea (2) (4 g, 0.05 mol), ethyl acetoacetate (1) (6.3 mL, 0.05 mol), sodium methoxide (5.9 g, 0.1 mol), and 47.4 mL of methanol. The reaction mixture was heated gently on the steam bath and dried in a hood for around 8 h. The residue was dissolved in 50 mL of hot water, and the resulting solution was then filtered after being treated with a few grams of activated carbon. The hot filtrate was carefully treated with 6.9 mL of glacial acetic acid. The thiouracil quickly precipitates, and it was filtered before being collected using a Buchner funnel. The wet solid filter cake was suspended in a boiling solution of 50 mL of water and 1 mL of glacial acetic acid. To remove any lumps, the slurry was properly mixed and agitated, and it was then kept in a refrigerator. 50 mL of cold water, divided into four to five portions, was used to filter and wash the product. The solid was dried to get the final product of 2-thio-6-methyluracil (3).

2-Thio-6-methyluracil (3)

State:white powder; Yield: 82%; Melting point: 328-330°C; R_f 0.34 (cyclohexane: ethylacetate, 6:4V/V); IR (ν cm^{-1}): 3003 (CH_3), 1624 (C_5=C_6), 1161, 870 (C=S); ^{1}HNMR (DMSO-d6) 2.10 (s, 3H, -CH_3), 5.62 (s, 1H, -CH), 12.22 (s, 2H, -SH and -OH)

Table I: Physical characteristics of synthesized compounds (7a-j)

Comp. No.	Molecular formula	Colour	Melting point (°C)	R_f*	Yield (%)
7a	$C_{14}H_9BrN_2O_2S$	Yellow	220-224	0.38	80.6
7b	$C_{14}H_9ClN_2O_2S$	Brown	270-274	0.40	81.7
7c	$C_{14}H_9FN_2O_2S$	Light brown	246-250	0.46	77.5
7d	$C_{15}H_{12}N_2O_2S$	Yellow	240-244	0.42	79.6
7e	$C_{15}H_{12}N_2O_3S$	Yellowish orange	230-234	0.39	78.7
7f	$C_{16}H_{15}N_3O_2S$	Dark red	244-248	0.49	77.8
7g	$C_{14}H_9N_3O_4S$	Light yellow	236-240	0.43	80.9
7h	$C_{15}H_9N_3O_2S$	Dull yellow	276-280	0.35	75.6
7i	$C_{15}H_{12}N_2O_4S$	Yellowish orange	232-236	0.50	78.9
7j	$C_{14}H_{10}N_2O_2S$	Light yellow	250-254	0.48	82.5

**Petroleum ether: Ethylacetate: Methanol 6:3:1*

Table II: *In vitro* antimicrobial screening

Comp. No.#	Zone of inhibition (mm)	
	***E. coli* (MTCC 40)**	***S. aureus* (MTCC 87)**
7a	24.49 ± 0.47	23.67 ± 0.36
7b	23.90 ± 0.63	22.32 ± 0.58
7c	24.49 ± 0.47	23.04 ± 0.20
7d	16.11 ± 0.36	15.49 ± 0.61
7e	15.03 ± 0.17	14.80 ± 0.66
7f	24.02 ± 0.56	22.00 ± 0.47
7g	15.92 ± 0.46	14.90 ± 0.17
7h	13.80 ± 0.10	11.06 ± 0.27
7i	12.03 ± 0.19	11.13 ± 0.18
7j	12.40 ± 0.57	12.01 ± 0.51
Standard	28.71±0.58*	27.48±0.17*

*#at a concentration of 100 µg mL^{-1}, Standard (Ciprofloxacin); *± SD (n=3) mean of zone of inhibition in mm*

Synthesis of various derivatives of 2-(4-substitutedbenzylidene)-7-methyl-2*H*-thiazolo[3,2-*a*] pyrimidine-3,5-dione (7a-j) A mixture of (3)(0.7 g, 0.005 mol), chloroacetic acid (4) (0.5 g, 0.005 mol), anhydrous sodium acetate (5) (1g, 0.012 mol) and the substituted benzaldehyde (6), was refluxed in a mixture of 15 mL of glacial acetic acid and 7.5 mL of acetic anhydride for 3 h. The reaction mixture was poured into water. The precipitates were filtered off, washed with water, dried and crystallized from the proper solvent to produce 2-(4-substituted benzylidene)-7-methyl-2*H*-thiazolo [3,2-*a*]pyrimidine-3,5-diones (7a-j).

2-(4-Bromobenzylidene)-7-methyl-2*H*-thiazolo[3,2-*a*]pyrimidine-3,5-dione (7a): State: Yellow powder; Yield: 80.6%; Melting point: 220-224°C; R_f 0.38 (petroleum ether: ethylacetate: methanol 6:3:1V/V/V); IR (ν cm^{-1}):1756, 1674 (–C=O), 1640 (C=C), 1070 (–C-Br); ^{1}HNMR ($CDCl_3$) 2.30 (s, 3H, CH_3), 6.11 (s, 1H, pyrimidine-H_6), 7.44-7.67 (d, 4H, Ar-H), 7.99 (s, 1H, =CH); MS *m/z* 185.0.

2-(4-Chlorobenzylidene)-7-methyl-2*H*-thiazolo[3,2-*a*]pyrimidine-3,5-dione (7b): State: Brown powder; Yield: 81.7%; Melting point: 270-274°C; R_f 0.40 (petroleum ether: ethylacetate: methanol 6:3:1V/V/V); IR (ν cm^{-1}):1752, 1680 (–C=O), 1639 (C=C), 1087 (–C-Cl); ^{1}HNMR ($CDCl_3$) 2.30 (s, 3H, CH_3), 6.11 (s, 1H, pyrimidine-H_6), 7.44-7.67 (d, 4H, Ar-H), 7.99 (s, 1H, =CH).

2-(4-Fluorobenzylidene)-7-methyl-2*H*-thiazolo[3,2-*a*]pyrimidine-3,5-dione (7c): State: Light brown powder; Yield: 77.5%; Melting point: 246-250°C; R_f 0.46 (petroleum ether: ethylacetate: methanol 6:3:1V/V/V); IR (ν cm^{-1}):1758, 1664 (–C=O), 1637 (C=C), 1233 (–C-Fl); ^{1}HNMR ($CDCl_3$) 2.29 (s, 3H, CH_3), 6.11 (s, 1H, pyrimidine-H_6), 7.24-7.5 (d, 4H, Ar-H), 8.03 (s, 1H, =CH).

7-Methyl-2-(4-methylbenzylidene)-2*H*-thiazolo[3,2-*a*]pyrimidine-3,5-dione (7d): State:Yellow powder; Yield: 79.6%; Melting point: 240-244°C; R_f 0.42 (petroleum ether: ethylacetate: methanol 6:3:1V/V/V); IR (ν cm^{-1}): 1760, 1685 (–C=O), 1634 (C=C); ^{1}HNMR ($CDCl_3$) 2.29-2.68 (s, 6H, $(CH_3)_2$), 6.10 (s, 1H, pyrimidine-H_6), 7.34-7.48 (d, 4H, Ar-H), 8.06 (s, 1H, =CH).

2-(4-Methoxybenzylidene)-7-methyl-2*H*-thiazolo[3,2-*a*]pyrimidine-3,5-dione (7e): State:Yellowish orange powder; Yield: 78.7%; Melting point: 230-234°C; R_f 0.39 (petroleum ether: ethylacetate: methanol 6:3:1V/V/V); IR (ν cm^{-1}): 1748, 1660 (–C=O), 1637 (C=C); ^{1}HNMR ($CDCl_3$) 2.28 (s, 3H, CH_3), 3.87-3.88 (s, 3H, OCH_3), 6.10 (s, 1H, pyrimidine-H_6), 7.01-7.54 (d, 4H, Ar-H), 8.02 (s, 1H, =CH).

2-(4-(Dimethylamino)benzylidene)-7-methyl-2*H*-thiazolo[3,2-*a*]pyrimidine-3,5-dione (7f): State:Dark red Yield: 77.8%; Melting point: 244-248°C; R_f 0.49 (petroleum ether: ethylacetate: methanol 6:3:1V/V/V); IR (ν cm^{-1}):1749, 1691 (–C=O), 1644 (C=C); ^{1}HNMR ($CDCl_3$) 2.27-2.66 (s, 3H, CH_3), 3.03-3.09 (s, 6H, N $(CH_3)_2$), 6.06 (s, 1H, pyrimidine-H_6), 6.74-7.46 (d, 4H, Ar-H), 7.98 (s, 1H, =CH).

7-Methyl-2-(4-nitrobenzylidene)-2*H*-thiazolo[3,2-*a*]pyrimidine-3,5-dione (7g): State:Light yellow; Yield: 80.9%; Melting point: 236-240°C; R_f 0.43 (petroleum ether: ethylacetate: methanol 6:3:1V/V/V); IR (ν cm^{-1}):1760, 1694 (–C=O), 1643 (C=C), 1517 (asymmetric stretch), 1341(symmetric stretch) NO_2 group; ^{1}HNMR ($CDCl_3$) 2.32 (s, 3H, CH_3),6.15 (s, 1H, pyrimidine-H_6), 7.75-8.38 (d, 4H, Ar-H), 8.09 (s, 1H, =CH).

4-((7-Methyl-3,5-dioxo-3,5-dihydro-2*H*-thiazolo[3,2-*a*]pyrimidin-2-ylidene)methyl) benzonitrile (7h): State:Dull yellow; Yield: 75.6%; Melting point: 276-280°C; R_f 0.35 (petroleum ether: ethylacetate: methanol 6:3:1V/V/V); IR (ν cm^{-1}):2223 (–CN), 1754, 1673 (–C=O), 1644 (C=C); ^{1}HNMR ($CDCl_3$) 2.31(s, 3H, CH_3), 6.14 (s, 1H, pyrimidine-H_6), 7.67-7.82 (d, 4H, Ar-H), 8.04 (s, 1H, =CH).

Table III: *In vitro* percent control growth of Human Myelomonocytic Leukemia cell line U-937 at different molar drug concentrations

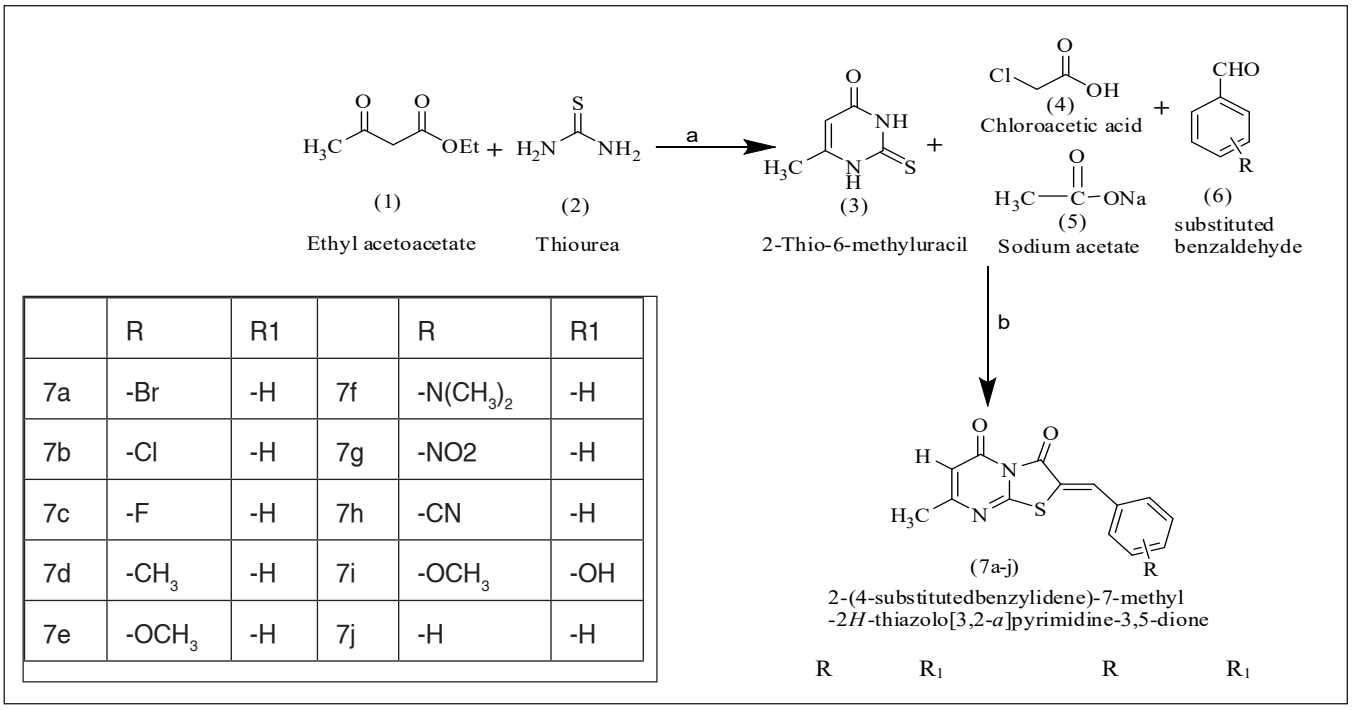
Comp. No.	Drug concentrations (µg mL^{-1})															
	(Experiment 1)				(Experiment 2)				(Experiment 3)				Average % control growth			
	10	20	40	80	10	20	40	80	10	20	40	80	10	20	40	80
7a	30.8	-4.8	-21.9	-15.3	31.3	17.3	-28.0	1.1	55.8	-11.0	-16.6	-24.3	39.3	0.5	-22.2	-12.8
7b	29.6	-21.0	-18.5	-34.0	30.7	4.5	-33.7	-10.1	27.9	-13.8	-3.5	-5.9	29.4	-10.1	-18.5	-16.7
7c	21.2	-6.2	-12.8	-28.3	43.5	3.8	-18.4	-18.4	41.4	-15.7	-11.3	6.4	35.3	-6.0	-14.2	-13.4
7d	15.6	-8.6	-14.5	-8.3	56.7	21.4	2.1	-6.1	67.3	23.4	15.6	5.1	46.6	12.1	1.1	-3.1
7e	-16.9	-24.3	-33.2	-27.6	40.4	2.1	5.4	3.2	35.1	2.3	11.5	7.5	19.6	-6.6	-5.4	-5.6
7f	38.0	24.7	24.5	16.5	60.0	50.0	74.6	41.2	48.5	43.8	57.5	41.1	48.8	39.5	52.2	32.9
7g	-9.2	-11.7	-13.4	-9.5	13.6	-11.0	4.3	9.2	4.1	-26.8	-9.5	-3.6	2.8	-16.5	-6.2	-1.3
7h	52.8	2.9	-21.3	-26.4	9.1	-6.1	-17.6	-35.6	24.0	-11.5	-25.8	-30.7	28.6	-4.9	-21.6	-30.9
7i	60.2	1.2	-23.1	-24.6	42.5	25.7	-8.0	-6.5	37.0	-18.7	-12.0	-18.8	46.6	2.7	-14.3	-16.6
7j	50.1	2.0	-4.1	-24.2	43.4	11.6	-6.9	1.1	3.3	-24.3	-23.9	-5.8	32.3	-3.6	-11.6	-9.7
ADR	30.0	-4.6	-17.6	-11.6	12.6	11.7	-24.6	11.0	4.7	-29.5	-28.7	-15.6	15.7	-7.5	-23.6	-5.4

2-(3-Hydroxy-4-methoxybenzylidene)-7-methyl-2*H*-thiazolo[3,2-*a*]pyrimidine-3,5-dione (7i): State: Yellowish orange; Yield: 78.9%; Melting point: 232-236°C; R_f 0.50 (petroleum ether: ethylacetate: methanol 6:3:1V/V/V); IR (ν cm^{-1}): 3748 (-O-H), 1755, 1693 (–C=O), 1639 (C=C); ^{1}HNMR ($CDCl_3$) 2.35 (s, 3H, CH_3),3.91 (s, 3H, OCH_3), 6.10 (s, 1H, pyrimidine-H_6), 7.08-7.27 (s, 3H, Ar-H), 7.93 (s, 1H, O-H), 7.97 (s, 1H, =CH).

2-Benzylidene-7-methyl-2*H*-thiazolo[3,2-*a*] pyrimidine-3,5-dione (7j): State:Light yellow; Yield: 82.5%; Melting point: 250-254°C; R_f 0.48 (petroleum ether: ethylacetate: methanol 6:3:1V/V/V); IR (ν cm^{-1}):1764, 1663 (–C=O), 1634 (C=C); ^{1}HNMR ($CDCl_3$) 2.30 (s, 3H, CH_3), 6.11 (s, 1H, pyrimidine-H_6), 7.51-7.57 (m, 5H, Ar-H), 8.08(s, 1H, =CH).

Antimicrobial screening by agar well diffusion method

For antibacterial activity against the Gram positive bacterium *S. aureus* (MTCC 87) and the Gram negative bacterium *E. coli* (MTCC 40), all the synthesised compounds were tested. The concentration level used for the initial screening was 100 g mL^{-1}. For antibacterial research, ciprofloxacin (100 g mL^{-1}) served as the reference medication. DMSO served as the adverse control. The zone of inhibition was measured in mm. The value of the inhibition zone is presented as mean



	R	R1		R	R1
7a	-Br	-H	7f	$-N(CH_3)_2$	-H
7b	-Cl	-H	7g	-NO2	-H
7c	-F	-H	7h	-CN	-H
7d	$-CH_3$	-H	7i	$-OCH_3$	-OH
7e	$-OCH_3$	-H	7j	-H	-H

Fig. 1: Reaction scheme for the synthesis of 2- Substituted benzylidene-7-methyl-*2H*-thiazolo[3,2-a]pyrimidine-3, 5-diones

Reagents and Conditions: a) Sodium methoxide, methanol, heat, 8 h b) Glacial CH_3COOH, acetic anhydride, reflux 3 h

Table IV: TGI, LC_{50} and GI_{50} of the synthesized compounds against Human Myelomonocytic Leukemia cell line U-937

Comp. No.	LC_{50} (µg mL^{-1})	TGI (µg mL^{-1})	GI_{50} (µg mL^{-1})
7a	15.9	4.8	<10
7b	17.1	3.4	<10
7c	17.5	4.6	<10
7d	19.5	7.8	<10
7e	33.4	4.8	<10
7f	77.8	38.5	<10
7g	88.2	16.8	<10
7h	12.3	3.2	<10
7i	14.5	5.3	<10
7j	20.1	5.1	<10
ADR	32.7	1.2	<10

SD (n=3) (mean of the inhibition zone), which is used to compare the antibacterial activity of test and standard compounds.

ANTICANCER EVALUATION

In vitro anti-cancer screening

Human myelomonocytic leukaemia cell line U-937 was employed as the anticancer screening test for all synthesised compounds to determine their capacity to inhibit cell proliferation. The cell line was obtained from the National Cancer Institute (NCI) of the USA. Because of its anticancer properties, andriamycin was often the recommended drug. The experimenting material used was dimethyl sulfoxide (DMSO). According to the SRB testing protocol, each derivative was tested *in vitro* at 4 dose levels (10 g mL^{-1}, 20 g mL^{-1}, 40 g mL^{-1}, and 80 g mL^{-1}).

The percent growth at each of the drug concentration levels was computed utilizing the seven absorbance, measurements, namely, time zero (Tz), control growth (C), and test growth in the presence of drug at the five concentration levels (Ti). For concentrations where Ti>/=Tz, the percent growth inhibition was computed as[(Ti-Tz)/(C-Tz)] x 100.

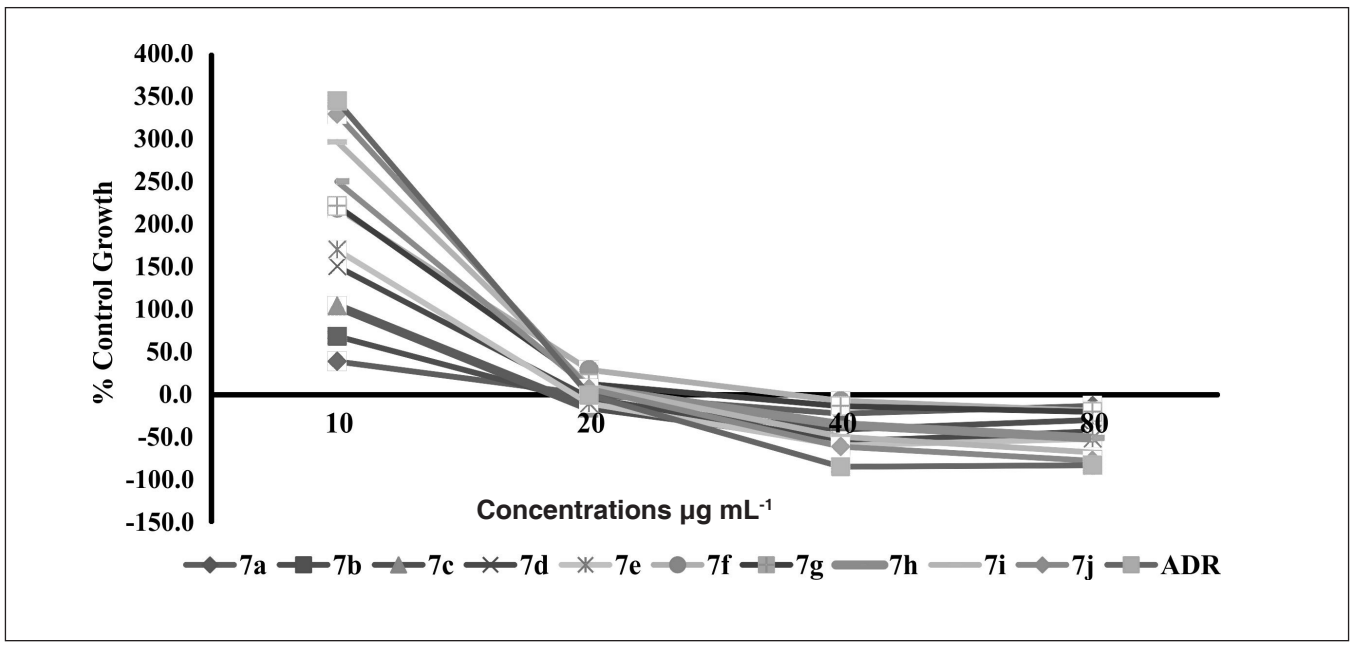


Fig. 2: Graph showing % control growth against the drug concentrations for compounds 7a-7j and standard andriamycin

[(Ti-Tz)/Tz] x 100

(for concentrations where Ti<Tz).

For each drug, the three dose-response parameters, GI_{50}, total growth inhibition (TGI), and LC_{50}, were computed.

RESULTS AND DISCUSSION

The synthesis of various 2-(4-substitutedbenzylidene)-7-methyl-2*H*-thiazolo[3,2-a]pyrimidine-3,5-diones was done in accordance with the suggested technique (Fig. 1). The yield of the aforementioned derivatives was shown to be between 75.6 and 82.5 %. The uncorrected melting points were in the range of 220-280 °C. Using various solvents and detecting systems, the R_f values were found to be in the range of 0.35 to 0.50 (Table I). In the experimental part, spectrum information of the synthetic derivatives is provided.

Antimicrobial activity

Among all the derivatives in the series 7a-j, the halogenated and amino derivatives exhibited potent antibacterial activity (Table II). As compared to other compounds in the series, compounds 7a, 7b, 7c and 7f exhibited better activity against both the tested strains, while compounds 7d, 7e and 7g activities were found to be moderate. The other substances had only marginal activity against the examined species.

Anticancer drug screening

To ascertain whether any compounds had a growth-inhibitory impact, all the synthesised substances were tested against the human myelomonocytic leukaemia cell line U-937. Each derivative was examined *in vitro* at 4 dose levels (10 g mL^{-1}, 20 g mL^{-1}, 40 g mL^{-1}, and 80 g mL^{-1}) according to the SRB assay procedure.

The synthesized 2-(4-substitutedbenzylidene)-7-methyl-2*H*-thiazolo[3,2-*a*]pyrimidine-3,5-diones exhibited encouraging anticancer results. The order for the % control growth inhibition of U-937 was found to be 7h>7b>7a>7f>7e>7i>7j>7d>7f (10 µg mL^{-1}, 20 µg mL^{-1}, 40 µg mL^{-1}, 80 µg mL^{-1}) as indicated in Table III. The compounds 7h, 7a, 7b, 7e, 7i and 7j exhibited total growth inhibition (TGI) in the concentration range 3.2-5.3 µg mL^{-1} in comparison to 1.2 µg mL^{-1} for andriamycin (Table IV). The results pertaining to GI_{50} and LC_{50} have been presented in the Table IV and Fig. 2. The results clearly indicate that the derivatives have the potential to act as anticancer agents. The substitution at 4-position of benzylidene had variable effect on the activity. The electron withdrawing substituent like –CN, -Cl, -Br, -F and $-OCH_3$ had better activity than the unsubstituted and electron donating substituents like $–CH_3$ and $–N(CH_3)_2$ groups.

The order for the % control growth inhibition of U-937 was found to be (at 40 µg mL^{-1}) 7a>7b>7j = 7c >7g while 7a is most active due to the presence of electron

withdrawing group and at 80 µg mL^{-1}) 7h and 7i are active compounds while 7h is more active than 7i. 7f is inactive due to the presence of electron donating group.

CONCLUSION

In conclusion, a total of ten 2-(4-substituted benzylidene)-7-methyl-2*H*-thiazolo[3, 2-a] pyrimidine-3,5-diones (7a-7g) have been synthesized and evaluated for their anti-cancer as well as anti-bacterial potential. Among the synthesized heterocycles, compound 7a and 7b were the most potent compounds with good results for both the assays. The thiazolopyrimidine derivative 7a, represents a promising structure for the development of new compounds with better activity and for future *in vivo* analysis. All the other synthesized compounds can be further explored by utilizing various other substituted precursors and studying their structure activity relationship.

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