Original Article

Synthesis, Characterization, Antimicrobial And Anticancer Evaluation Of (E)-2-(Benzylideneamino)-4-Methyl-N-(4-Oxo-2-(Substituted Phenyl)Thiazolidin-3-Yl)Thiazole-5-Carboxamide Derivatives

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Abstract

Thiazolidinone derivatives (T1-T20) were synthesized and structures of these compounds were elucidated by IR, and ^{1}H NMR. Synthesized compounds were screened for antibacterial activity against Gram-negative (E. coli) and Gram-positive (S. aureus and B. subtilis) bacteria, antifungal activity against pathogenic fungal strains (A. niger and C. albicans and anticancer activity. Some of the compounds exhibited promising antimicrobial and anticancer activity.

Keywords: 4-Thiazolidinone, Characterization, Antimicrobial, Anticancer,

Introduction

The treatment of infectious diseases remains one of the most important and challenging areas of global public health. Infections caused by microbes are one of the leading causes of death worldwide, especially in low-income countries. The World Health Organization (WHO) named three infectious diseases: lower respiratory tract infections, diarrheal diseases and tuberculosis in the list of the top ten leading causes of death worldwide in 2016. Although various antimicrobial and antifungal agents have been discovered over the last few decades, the significant need to search of new effective antimicrobials remains a major concern due to the rapid increase in microbial resistance and the emergence of multidrug-resistant pathogens [1].

Cancer encompasses many disease states generally characterized by abnormally proliferating cells and is a serious and often fatal disease. However, the effect of anticancer drugs on solid tumors was small. As the response of

solid tumors to available anticancer chemotherapy has been reduced, new drugs with improved efficacy are desired [2].

4-Thiazolidinone scaffolds belong to privileged structures in drug design. 4-thiazolidinone derivatives have continued to be the focus of research by medicinal chemists and have once again returned to the world pharmaceutical market. Thus, the 5-ylidene derivative of 2-(alkyl)imino-4-thiazolidinone Ponesimod (Ponvory) was approved by the FDA in 2021 as a potential drug for the treatment of multiple sclerosis and psoriasis. [3] Thiazolidin-4-one derivatives are known to exhibit diverse biological activities such as antimicrobial[4–5] anticancer[6-8] analgesic and anti-inflammatory [9] antiviral, [10-11], antioxidant[12] antidiabetic [13], anti-convulsant [14] activities.

In view of the above facts and continuing our research in the field of antimicrobial anticancer agents and previously synthesized new derivatives of 4-thiazolidinones [15-16], we hereby report the synthesis, antimicrobial and anticancer evaluation of 4-thiazolidinone derivatives.

Chemistry: Thiazole Schiff bases were prepared by the reaction of (E)-2-(benzylideneamino)-4-methylthiazole-5-carbohydrazide with corresponding aromatic aldehydes. Furthermore, the reaction of these Schiff bases with thioglycolic acid gives the 2-substituted 4-thiazolidinone derivatives (Scheme 1). Thiazolidinone derivatives were characterized on the basis of spectral and analytical studies.

Experimental

Melting points were determined in open capillary and are uncorrected. FT-IR spectra were recorded using Perkin-Elmer spectrometer. 1H NMR spectra were recorded on Brucker Advance II 400 spectrometer in DMSO solvent by using TMS as internal standard. Chemical shift (δ) values are reported in ppm units, relative to TMS as internal standard. Mass spectra were recorded on GC-MS Mass spectrometer. The reactions were monitored by thin layer chromatography (TLC) using silica coated plates (Merck).

General Procedure for the synthesis of titled compounds (T1-T20).

Synthesis of ethyl 2-amino-4-methyl-1,3-thiazole-5-carboxylate:

To a mixture of anhydrous ethanol (100 mL) and thiourea (0.098 M), ethyl-2-chloro acetoacetate (0.097M) was added drop-wise under constant stirring at room temperature. Once addition of ethyl-2-chloro acetoacetate is completed, reaction mixture was heated at 70–80 °C for 15 min. Then reaction mass was cooled to room temperature, and the solid precipitate was isolated, washed with 100 mL of cold ethanol and further washed with saturated sodium bicarbonate solution to obtain white solid which was finally dried under vacuum at 50 °C for 8 h.

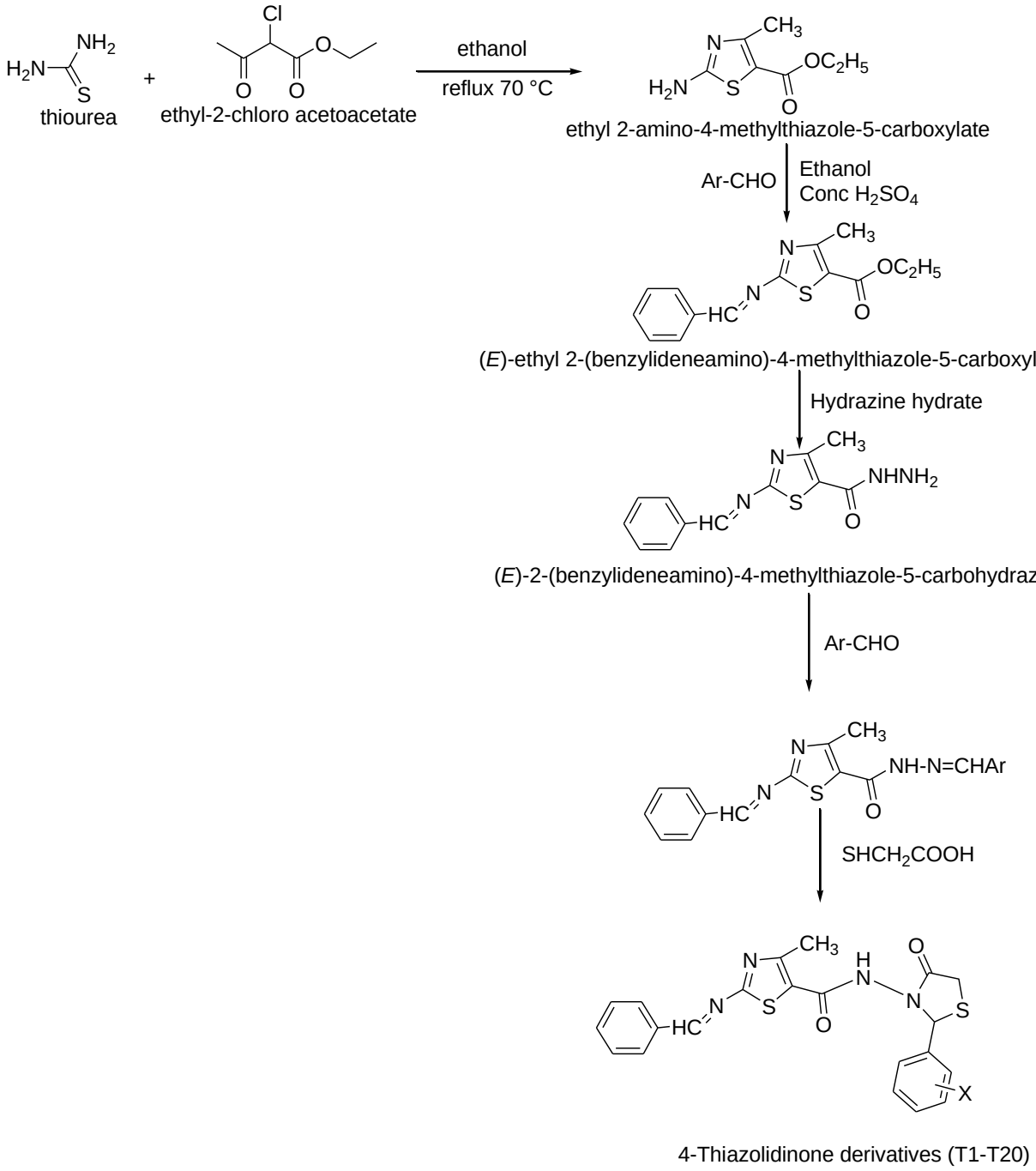
Synthesis of (E)-ethyl 2-(benzylideneamino)-4-methylthiazole-5-carboxylate: To a solution of benzaldehyde (0.001M) in 50 mL of methanol, ethyl 2-amino-4-methyl-1,3-thiazole-5-carboxylate (3) (0.0012 M) was added with a few drops of sulfuric acid and refluxed for 3 hours or till the completion of reaction. A solid precipitate obtained was filtered, washed with water, dried and further recrystallized with ethanol to give solid products. The progress of the reaction and purity of the compound were checked by TLC, using toluene: ethyl acetate: formic acid (5:4:1) as mobile phase.

Synthesis of (E)-2-(benzylideneamino)-4-methylthiazole-5-carbohydrazide: A mixture of (0.2 M) (E)-ethyl 2-(benzylideneamino)-4-methylthiazole-5-carboxylate and excess of hydrazine hydrate (0.30 M, 15 ml), ethanol (250 ml) was refluxed for about 3 h and cooled. The solid was separated by filtration and recrystallized from ethanol to afford (E)-2-(benzylideneamino)-4-methylthiazole-5-carbohydrazide.

Synthesis of hydrazone derivatives.

A mixture of (0.025 M) (E)-2-(benzylideneamino)-4-methylthiazole-5-carbohydrazide (3) and required aromatic aldehydes (0.025 M) was refluxed in methanol (50 ml) in the presence of a catalytic amount of glacial acetic acid for about 2 h. The mixture was cooled; the solid was separated by filtration and recrystallized from methanol to give the corresponding hydrazones.

Synthesis of 2,3-disubstituted-4-thiazolidinone: A mixture of (0.015 M) hydrazone derivatives and required amount of thioglycolic acid (0.015 M, 1.40 ml) in DMF (50 ml), containing a pinch of anhydrous $ZnCl_2$ was refluxed for about 6 h. The reaction mixture was cooled and poured on to crushed ice. The solid thus obtained was filtered, washed with water, and the product was recrystallized from rectified spirit [17]. Synthetic pathway for formation of title compounds is presented in Scheme 1.



Scheme 1

Table-1 Physical data of 4-thiazolidinone derivatives

Comp.	M. Formula	X	M. Pt. (^{o}C)	M. Wt.	R_f value*	% yield
T1	**$C_{24}H_{24}N_4O_5S_2$**	3,4,5-methoxy benzaldehyde	113-115	**512.60**	0.66	71
T2	**$C_{22}H_{20}N_4O_3S_2$**	3-methoxy benzaldehyde	139-141	**452.55**	0.63	69
T3	**$C_{21}H_{18}N_4O_3S_2$**	2-hydroxy benzaldehyde	157-159	**438.52**	0.70	87
T4	**$C_{21}H_{17}N_5O_4S_2$**	3-nitro benzaldehyde	175-177	**467.52**	0.76	74
T5	**$C_{21}H_{17}ClN_4O_2S_2$**	3-chloro benzaldehyde	201-203	**456.97**	0.73	76
T6	**$C_{22}H_{20}N_4O_2S_2$**	4-methyl benzaldehyde	174-176	**436.55**	0.70	72
T7	**$C_{21}H_{17}BrN_4O_2S_2$**	4-bromo benzaldehyde	189-191	**501.42**	0.65	89
T8	**$C_{23}H_{23}N_5O_2S_2$**	4-dimethyl amino benzaldehyde	163-165	**465.59**	0.75	66
T9	**$C_{21}H_{17}N_5O_4S_2$**	4-nitro benzaldehyde	205-207	**467.52**	0.70	72
T10	**$C_{21}H_{17}FN_4O_2S_2$**	4-fluorobenzaldehyde	245-247	**440.51**	0.65	67
T11	**$C_{21}H_{17}ClN_4O_2S_2$**	4-chloro benzaldehyde	190-192	**456.97**	0.63	69
T12	**$C_{25}H_{27}N_5O_2S_2$**	4-diethylamino benzaldehyde	186-188	**493.64**	0.73	74
T13	**$C_{22}H_{20}N_4O_4S_2$**	4-hydroxy-3-methoxy benzaldehyde	197-199	**468.55**	0.60	61
T14	**$C_{21}H_{17}FN_4O_2S_2$**	3-fluorobenzaldehyde	212-214	**440.51**	0.65	75
T15	**$C_{22}H_{20}N_4O_3S_2$**	2-methoxy benzaldehyde	178-180	**452.55**	0.78	63
T16	**$C_{21}H_{16}C_{l2}N_4O_2S_2$**	2,4-dichloro benzaldehyde	222-224	**491.41**	0.81	65
T17	**$C_{21}H_{17}BrN_4O_2S_2$**	3-bromo benzaldehyde	214-216	**501.42**	0.69	62
T1 8	**$C_{21}H_{18}N_4O_2S_2$**	Benzaldehyde	185-187	**422.52**	0.62	74
T19	**$C_{21}H_{17}ClN_4O_2S_2$**	2-chloro benzaldehyde	193-195	**456.97**	0.66	84
T20	**$C_{21}H_{17}BrN_4O_2S_2$**	2-bromo benzaldehyde	156-158	**501.42**	0.59	67

Solvent:Benzene

Spectral data:

(E)-2-(benzylideneamino)-4-methyl-N-(4-oxo-2-(3,4,5-trimethoxyphenyl)thiazolidin-3-yl)thiazole-5-carboxamide (T1) IR (KBr, cm^{-1}): 3483(NH), 3012 (C-H Ar), 2988 (C-H str., -CH_3), 1739 (C=O), 1692 (C=N str), 1649 (C=C Ar), 1391 (C-N), 1234(C–O–C str), 723(C-S); ^{1}H NMR (DMSO-d6, 400 MHz): 8.63-8.53 (m, 7H, ArH), 8.51(s, 1H, CH=N), 7.46 (s, 1H, -NCHS), 3.72 (s, 2H, CH_2), 3.35 (s, 9H, –OCH_3), 2.50 (s, 1H, CH_3 thiazole),

(E)-2-(benzylideneamino)-N-(2-(3-methoxyphenyl)-4-oxothiazolidin-3-yl)-4-methylthiazole-5-carboxamide (T2) IR (KBr, cm^{-1}): 3412(NH), 2960 (C-H Ar), 2931 (C-H str., -CH_3), 1592 (C=N str), 1529 (C=C Ar), 1387 (C-N), 1266 (C–O–C str), 719(C-S); ^{1}H NMR (DMSO-d6, 400 MHz): 7.57-7.20 (m, 9H, ArH), 7.01(s, 1H, CH=N), 6.98 (s, 1H, -NCHS), 3.84 (s, 2H, CH_2), 3.50 (s, 3H, –OCH_3), 2.50 (s, 1H, CH_3 thiazole),

(E)-2-(benzylideneamino)-N-(2-(2-hydroxyphenyl)-4-oxothiazolidin-3-yl)-4-methylthiazole-5-carboxamide (T3) IR (KBr, cm^{-1}): 3651(OH), 3301(NH), 2996 (C-H Ar), 2822 (C-H str., -CH_3), 1713 (C=O), 1698 (C=N str), 1649 (C=C Ar), 1397 (C-N), 731(C-S); ^{1}H NMR (DMSO-d6, 400 MHz): 7.54-7.13 (m, 9H, ArH), 7.00(s, 1H, CH=N), 6.91 (s, 1H, -NCHS), 5.81(s, 1H, OH), 3.49 (s, 2H, CH_2), 2.38 (s, 1H, CH_3 thiazole).

(E)-2-(benzylideneamino)-4-methyl-N-(2-(3-nitrophenyl)-4-oxothiazolidin-3-yl)thiazole-5-carboxamide (T4) IR (KBr, cm^{-1}): 3464(NH), 3079 (C-H Ar), 2962 (C-H str., -CH_3), 1701 (C=O), 1639 (C=N str), 1602 (C=C Ar), 1519 (N–O str, NO2), 1377 (C-N), 711(C-S); ^{1}H NMR (DMSO-d6, 400 MHz): 8.62-7.28 (m, 9H, ArH), 7.00(s, 1H, CH=N), 6.79 (s, 1H, -NCHS), 3.73 (s, 2H, CH_2), 2.83 (s, 1H, CH_3 thiazole),

(E)-2-(benzylideneamino)-N-(2-(3-chlorophenyl)-4-oxothiazolidin-3-yl)-4-methylthiazole-5-carboxamide(T5) IR (KBr, cm^{-1}): 3335(NH), 3032 (C-H Ar), 2969 (C-H str., -CH_3), 1739 (C=O), 1691 (C=N str), 1609 (C=C Ar), 1393 (C-N), 783(C–Cl), 715(C-S); ^{1}H NMR (DMSO-d6, 400 MHz): 8.69-7.15 (m, 9H, ArH), 7.00(s, 1H, CH=N), 6.77 (s, 1H, -NCHS), 3.83 (s, 2H, CH_2), 2.88 (s, 1H, CH_3 thiazole),

(E)-2-(benzylideneamino)-4-methyl-N-(4-oxo-2-p-tolylthiazolidin-3-yl)thiazole-5-carboxamide(T6) IR (KBr, cm^{-1}): 3476(NH), 3200 (C-H Ar), 1699 (C=O), 1628 (C=N str), 1294 (C-N), 750(C-S); ^{1}H NMR (DMSO-d6, 400 MHz): 9.36-7.30 (m, 9H, ArH), 7.14(s, 1H, CH=N), 7.02 (s, 1H, -NCHS), 3.41 (s, 2H, CH_2), 3.12 (s, 3H, CH_3), 2.49 (s, 1H, CH_3 thiazole),

(E)-2-(benzylideneamino)-N-(2-(4-bromophenyl)-4-oxothiazolidin-3-yl)-4-methylthiazole-5-carboxamide(T7) IR (KBr, cm^{-1}): 3317(NH), 3036 (C-H Ar), 2934 (C-H str., -CH_3), 1673 (C=O), 1637 (C=N str), 1539 (C=C Ar), 1390 (C-N), 758(C-S) 648 (Br); ^{1}H NMR (DMSO-d6, 400 MHz): 9.06-8.00 (m, 9H, ArH), 7.71(s, 1H, CH=N), 7.47 (s, 1H, -NCHS), 3.52 (s, 2H, CH_2), 2.50 (s, 1H, CH_3 thiazole).

(E)-2-(benzylideneamino)-N-(2-(4-(dimethylamino)phenyl)-4-oxothiazolidin-3-yl)-4-methylthiazole-5-carboxamide (T8) IR (KBr, cm^{-1}): 3310 (NH), 3077 (C-H Ar), 2990 (C-H str., -CH_3), 1688 (C=O), 1636 (C=N str), 1602 (C=C Ar), 1349 (C-N), 757(C-S); ^{1}H NMR (DMSO-d6, 400 MHz): 8.27-8.00 (m, 9H, ArH), 7.84(s, 1H, CH=N), 6.98 (s, 1H, -NCHS), 3.55 (s, 2H, CH_2), 3.35 (s, 9H, –OCH_3), 2.51 (s, 1H, CH_3 thiazole), 2.49 (s, 6H, N $(CH3)_2$).

(E)-2-(benzylideneamino)-4-methyl-N-(2-(4-nitrophenyl)-4-oxothiazolidin-3-yl)thiazole-5-carboxamide (T9) IR (KBr, cm^{-1}): 3419(NH), 3060 (C-H Ar), 2923 (C-H str., -CH_3), 1700 (C=O), 1659 (C=N str), 1525 (N–O str, NO2), 1392 (C-N), 717(C-S); ^{1}H NMR (DMSO-d6, 400 MHz): 7.50-7.25 (m, 9H, ArH), 7.11(s, 1H, CH=N), 7.02 (s, 1H, -NCHS), 2.50 (s, 1H, CH_3 thiazole),

(E)-2-(benzylideneamino)-N-(2-(4-fluorophenyl)-4-oxothiazolidin-3-yl)-4-methylthiazole-5-carboxamide (T10) IR (KBr, cm^{-1}): 3448(NH), 3118 (C-H Ar), 2956 (C-H str., -CH_3), 1678 (C=O), 1588 (C=C Ar), 1328 (C-N), 1293 (C–F), 721 (C-S); ^{1}H NMR (DMSO-d6, 400 MHz): 7.39-7.26 (m, 9H, ArH), 7.24(s, 1H, CH=N), 6.98 (s, 1H, -NCHS), 3.55 (s, 2H, CH_2), 2.50 (s, 1H, CH_3 thiazole).

(E)-2-(benzylideneamino)-N-(2-(4-chlorophenyl)-4-oxothiazolidin-3-yl)-4-methylthiazole-5-carboxamide(T11) IR (KBr, cm^{-1}): 3447(NH), 3002 (C-H Ar), 2946 (C-H str., -CH_3), 1670 (C=O), 1588 (C=N str), 1566 (C=C Ar), 1393 (C-N), 761(C–Cl), 721(C-S); ^{1}H NMR (DMSO-d6, 400 MHz): 7.72-7.16 (m, 9H, ArH), 7.03(s, 1H, CH=N), 6.17 (s, 1H, -NCHS), 4.71 (s, 2H, CH_2), 2.50 (s, 1H, CH_3 thiazole),

(E)-2-(benzylideneamino)-N-(2-(4-(diethylamino)phenyl)-4-oxothiazolidin-3-yl)-4-methylthiazole-5-carboxamide (T12) IR (KBr, cm^{-1}): 3413(NH), 3068 (C-H Ar), 2836 (C-H str., $-CH_3$), 2730($-CH_2CH3$), 1697 (C=O), 1620 (C=N str), 1595 (C=C Ar), 1392 (C-N), 742(C-S); ^{1}H NMR (DMSO-d6, 400 MHz): 7.96-7.36 (m, 9H, ArH), 7.02(s, 1H, CH=N), 6.61 (s, 1H, -NCHS), 3.53 (s, 2H, CH_2), 3.36 (s, 1H, CH_3 thiazole), 2.50(m, 6H, CH_3), 2.08(m, 4H, CH_2).

(E)-2-(benzylideneamino)-N-(2-(4-hydroxy-3-methoxyphenyl)-4-oxothiazolidin-3-yl)-4-methylthiazole-5-carboxamide (T13) IR (KBr, cm^{-1}): 3648(OH), 3464(NH), 3110 (C-H Ar), 2925 (C-H str., $-CH_3$), 1723 (C=O), 1629 (C=N str), 1602 (C=C Ar), 1470 (C-N), 1287(C–O–C str), 711(C-S); ^{1}H NMR (DMSO-d6, 400 MHz): 8.03-7.54 (m, 8H, ArH), 7.52(s, 1H, CH=N), 7.28 (s, 1H, -NCHS), 3.69 (s, 2H, CH_2), 3.31 (s, 3H, $-OCH_3$), 2.74 (s, 1H, CH_3 thiazole),

(E)-2-(benzylideneamino)-N-(2-(3-fluorophenyl)-4-oxothiazolidin-3-yl)-4-methylthiazole-5-carboxamide (T14) IR (KBr, cm^{-1}): 3435(NH), 3007 (C-H Ar), 2875 (C-H str., $-CH_3$), 1749 (C=O), 1697 (C=N str), 1639 (C=C Ar), 1395 (C-N), 1298 (C–F), 724(C-S); ^{1}H NMR (DMSO-d6, 400 MHz): 7.62-7.35 (m, 9H, ArH), 7.19(s, 1H, CH=N), 7.07 (s, 1H, -NCHS), 2.49 (s, 2H, CH_2), 2.30 (s, 1H, CH_3 thiazole).

(E)-2-(benzylideneamino)-N-(2-(2-methoxyphenyl)-4-oxothiazolidin-3-yl)-4-methylthiazole-5-carboxamide (T15) IR (KBr, cm^{-1}): 3446(NH), 3107 (C-H Ar), 1634 (C=N str), 1533 (C=C Ar), 1394 (C-N), 1296(C–O–C str), 723(C-S); ^{1}H NMR (DMSO-d6, 400 MHz): 8.11-7.62 (m, 9H, ArH), 7.46(s, 1H, CH=N), 7.28 (s, 1H, -NCHS), 3.79 (s, 2H, CH_2), 3.36 (s, 3H, $-OCH_3$), 2.49 (s, 1H, CH_3 thiazole),

(E)-2-(benzylideneamino)-N-(2-(2,4-dichlorophenyl)-4-oxothiazolidin-3-yl)-4-methylthiazole-5-carboxamide (T16) IR (KBr, cm^{-1}): 3403 (NH), 3075 (C-H Ar), 2882 (C-H str., $-CH_3$), 1626 (C=N str), 1607 (C=C Ar), 1397 (C-N), 748(C–Cl), 717(C-S); ^{1}H NMR (DMSO-d6, 400 MHz): 9.50-9.14 (m, 8H, ArH), 8.10(s, 1H, CH=N), 6.97 (s, 1H, -NCHS), 3.78 (s, 2H, CH_2), 2.65 (s, 1H, CH_3 thiazole),

(E)-2-(benzylideneamino)-N-(2-(3-bromophenyl)-4-oxothiazolidin-3-yl)-4-methylthiazole-5-carboxamide (T17) IR (KBr, cm^{-1}): 3431(NH), 3025 (C-H Ar), 2887 (C-H str., $-CH_3$), 1658 (C=N str), 1564 (C=C Ar), 1388 (C-N), 784(C-S), 680 (Br); ^{1}H NMR (DMSO-d6, 400 MHz): 9.07-8.01 (m, 9H, ArH), 7.77(s, 1H, CH=N), 7.54 (s, 1H, -NCHS), 3.76 (s, 2H, CH_2), 2.50 (s, 1H, CH_3 thiazole),

(**E)-2-(benzylideneamino)-4-methyl-N-(4-oxo-2-phenylthiazolidin-3-yl)thiazole-5-carboxamide (T18)** IR (KBr, cm^{-1}): 3478(NH), 3013 (C-H Ar), 2818 (C-H str., $-CH_3$), 1746 (C=O), 1696 (C=N str), 1630 (C=C Ar), 1345 (C-N), 738(C-S); ^{1}H NMR (DMSO-d6, 400 MHz): 8.22-7.82 (m, 10H, ArH), 7.14(s, 1H, CH=N), 7.10 (s, 1H, -NCHS), 3.97 (s, 2H, CH_2), 2.50 (s, 1H, CH_3 thiazole),

(E)-2-(benzylideneamino)-N-(2-(2-chlorophenyl)-4-oxothiazolidin-3-yl)-4-methylthiazole-5-carboxamide (T19) IR (KBr, cm^{-1}): 3444(NH), 1742 (C=O), 1682 (C=N str), 1649 (C=C Ar), 1395 (C-N), 754(C–Cl), 719(C-S); ^{1}H NMR (DMSO-d6, 400 MHz): 9.21-7.49 (m, 9H, ArH), 7.33(s, 1H, CH=N), 7.02 (s, 1H, -NCHS), 3.74 (s, 2H, CH_2), 2.50 (s, 1H, CH_3 thiazole),

(E)-2-(benzylideneamino)-N-(2-(2-bromophenyl)-4-oxothiazolidin-3-yl)-4-methylthiazole-5-carboxamide (T20) IR (KBr, cm^{-1}): 3287(NH), 3178 (C-H Ar), 2963 (C-H str., $-CH_3$), 1673 (C=N str), 1590 (C=C Ar), 1394 (C-N), 771(C-S), 677 (Br); ^{1}H NMR (DMSO-d6, 400 MHz): 9.57-7.18 (m, 9H, ArH), 7.15(s, 1H, CH=N), 7.03 (s, 1H, -NCHS), 3.60 (s, 2H, CH_2), 2.50 (s, 1H, CH_3 thiazole),

Antimicrobial assay

The antimicrobial activity of synthesized compounds was performed against Gram-positive bacteria: Staphylococcus aureus MTCC 3160, Bacillus subtilis MTCC 441, Gram-negative bacterium: Escherichia coli MTCC 443 and fungal strains: Candida albicans MTCC 227 and Aspergillus niger MTCC 281 using tube dilution method[18] Dilutions of test and standard compounds were prepared in double strength nutrient broth – I.P. (bacteria) or Sabouraud dextrose broth

I.P. (fungi) The samples were incubated at 37 °C for 24 h (bacteria), at 25 °C for 7 d (A. niger) and at 37 °C for 48 h (C. albicans) and the results were recorded in terms of MIC[19].

Evaluation of anticancer activity

The anticancer activity of synthesized compounds **(T1-T20**) was determined against Hela cancer cell line. The cell line was cultured in RPMI 1640 (Sigma) supplemented with 10% heat inactivated fetal bovine serum (FBS) (PAA Laboratories) and 1% penicillin/streptomycin (PAA Laboratories). Culture was maintained in a humidified incubator at 37 °C in an atmosphere of 5% CO_2. Anticancer activity of synthesized compounds at various concentrations was assessed using 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) (Sigma) assay, as described by Mosmann, but with minor modification, following 72 h of incubation. Assay plates were read using a spectrophotometer at 520 nm. Data generated were used to plot a dose-response curve of which the concentration of test compounds required to kill 50% of cell population (IC_{50}) was determined. Anticancer activity was expressed as the mean IC_{50} of three independent experiments [20].

Table 2. In Vitro Antimicrobial Activity of the Title Compounds **(T1-T20**)

Compound	Minimum inhibitory concentration (µg ml^{-1})				
	Bacterial Strains			Fungal Strains	
	E. coli	S. aureus	B. subtilis	C. albicans	A. Niger
T1	25	12.5	25	25	12.5
T2	6.25	25	12.5	25	25
T3	25	12.5	25	25	25
T4	25	12.5	25	25	12.5
T5	25	12.5	25	25	12.5
T6	25	12.5	25	50	25
T7	25	25	3.12	50	25
T8	12.5	12.5	6.25	25	25
T9	50	25	3.12	25	12.5
T10	**1.56**	25	25	25	25
T11	25	12.5	25	25	12.5
T12	6.25	25	12.5	25	25
T13	25	12.5	25	25	25
T14	25	12.5	25	25	12.5
T15	25	25	25	12.5	**1.56**
T16	25	25	12.5	6.25	12.5
T17	12.5	**1.56**	**3.12**	**1.56**	12.5
T18	25	12.5	25	12.5	25
T19	25	25	25	12.5	25
T20	12.5	25	12.5	12.5	25
Ciprofloxacin (standard drug)	0.01	0.15	0.12	---	--
Clotrimazole (standard drug)	--	--	--	0.10	0.30

Table 2. Anticancer Activity of the Title Compounds **(T1-T20)**

S. No.	Compound	IC_{50}(µM)
1	T1	111.92
2	T2	241.93
3	T3	456.28
4	T4	112.70
5	T5	486.90
6	T6	536.30
7	T7	156.90
8	T8	118.45
9	T9	341.24
10	T10	69.13
11	T11	88.89
12	T12	231.29
13	T13	182.46
14	T14	284.20
15	T15	243.56
16	T16	411.26
17	T17	169.27
18	T18	190.32
19	**T19**	**65.98**
20	T20	157.90
STD Drug	**Doxorubicin**	**16.12**

RESULT AND DISCUSSION:

Antimicrobial activity

The antimicrobial activity of the synthesized compounds was determined by tube dilution method and the results are given in Table 2. Antimicrobial activity results revealed that compound **10** (MIC = 1.56 µg/ml) was found to be the most potent antibacterial agent against E. coli. In case of antifungal activity against A. niger, compound **15** (MIC = 1.56 µg/ml) was found to be the most potent antifungal agent. Compound 1**7** showed excellent antimicrobial activity against B. subtilis, S. aureus and C. albicans (MIC = 1.56 µg/ml, 3.12 µg/ml and 1.56 µg/ml respectively).

Thus, compound 1**7** was found to be the most potent antimicrobial agent among the synthesized 4-thiazolidinone derivatives and may be taken as a lead molecule for the development of novel antimicrobial agent.

The in vitro anticancer activity of the synthesized 4-thiazolidinone derivatives was determined against Hela cancer cell line using 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) assay, and the results are presented in Table 3. Anticancer activity results indicated that none of the synthesized compound exhibited better anticancer potential than the standard drug, Doxorubicin (IC_{50} = 16.12 µM) and compound **19** (IC_{50} = 65.98 µM) was found to be the most potent anticancer agent.

Conclusion:

A series of 4-thiazolidinones clubbed with thiazole nucleus has been synthesized and characterized by physicochemical and spectral means. The title compounds were screened for their in vitro antimicrobial and anticancer potentials. Results of antimicrobial and anticancer study revealed that compound 1**7** and **19** (IC_{50} = 65.98 µM) were found to be the most potent antimicrobial and anticancer activity respectively.

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