Original Article

SYNTHESIS, CHARACTERIZATION, ANTIMICROBIAL AND ANTICANCER EVALUATION 2-AZETIDINONE DERIVATIVES CLUBBED WITH THIAZOLE

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Abstract

A series of thiazole conjugated 2-azetidinones (1-20) was designed and synthesized. All synthesized derivative were evaluated for their antiproliferative potential against Hela cancer cell lines and antimicrobial activity respectively. Compounds 9 (IC_{50} = 58.86 µM) was found to be most potent anticancer agent. None of the substances was more effective than standard Doxorubicin. In case of antimicrobial activity, compounds exhibited good antimicrobial activity in comparison with standard drugs.

Keywords: 2-Azetidinone, Thiazole, Antimicrobial, Anticancer activity.

Introduction

The discovery, development and identification of biologically active antimicrobial compounds have gained a lot of importance in recent years, even though there are a considerable number of adverse effects. Medicinal chemists have always been tried to design drug molecules that possess maximum therapeutic application while having minimum toxicity profile. Moreover, because of excessive use of antibacterial antibiotics, immune-suppressants and cytotoxins, opportunistic mycosis has become prominent. To combat the increasing number of fungal pathogens and the growing burden of resistance, there is a need to develop new antimicrobial compounds [1].

Cancer is the second leading cause of death globally, accounting for an estimated 9.6 million deaths. Lung, prostate, colorectal, stomach and liver cancer are the most common types of cancer in men, while breast, colorectal, lung, cervical and thyroid cancer are the most common among womenMore than 70% of cancer deaths occurred in lowand middle-income countries. It is predicted that by 2030, two in five people globally will face a cancer diagnosis during their lifetime, and gains against infections and other conditions have led to increased life expectancy. It is high time to accelerate global cancer control through prevention, diagnosis, treatment and management, palliative care, and surveillance. Drug resistance and high toxicity are the major challenges in cancer therapy; hence, new drugs with good activity andminimum toxicity are required [2].

Azetidin-2-ones derivatives is well-known for their biological properties and when they are conjugated with other heterocyclic compound, exhibits various types of biological activities such as anticancer [3-5], antimicrobial[5-6], antimalarial[7-8], antitubercular[9-10], chymase inhibitory[11], antiviral[12], anticonvulsant[13] activities.

The synthesis, characterization antimicrobial and anticancer screening of 2-azetidinone ring were previously reported [14-15]. A series of 2-azetidinone derivatives (1 – 20) has been synthesized using a synthetic procedure outlined in Scheme 1, and their physicochemical properties are presented in Table 1

Chemistry: The Schiff's bases of thiazole was prepared by the reaction of (E)-2-(benzylideneamino)-4-methylthiazole-5-carbohydrazide with corresponding aromatic aldehydes. Further, reaction of these Schiff's bases with chloroacetyl chloride yield 2-azetidinone derivatives (Scheme 1). 2-Azetidinone derivatives were characterized on the basis of the spectral and analytical studies.

Experimental

Reaction progress was observed by thin layer chromatography. Melting points were determined in open capillary tubes on a Sonar melting point apparatus and are uncorrected. ^{1}H nuclear magnetic resonance (^{1}H NMR) spectra were determined by Bruker 400 MHz NMR spectrometer in appropriate deuterated solvents and are expressed in parts per million (δ, ppm) downfield from tetramethylsilane (internal standard) NMR data are given as multiplicity (s, singlet; d, doublet; t, triplet; m, multiplet) and number of protons. IR spectra were recorded on a Varian Resolutions Pro spectrophotometer in a KBr disc.

General Procedure for the synthesis of titled compounds (1-20).

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 (0.097 M) 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 (0.001 M) 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-azetidinone derivatives

(0.02M) Hydrazone derivatives was refluxed with triethylamine (0.02 M) and chloroacetyl chloride (0.02 M) in dimethylformamide (40 mL) for 3 h on water bath to yield 2-azetidinone derivative. After cooling, the solution

was poured on crushed ice to precipitate the crude product, which was recrystallized from rectified ethanol. [15]. Synthetic pathway for formation of title compounds is presented in Scheme 1.

Scheme 1

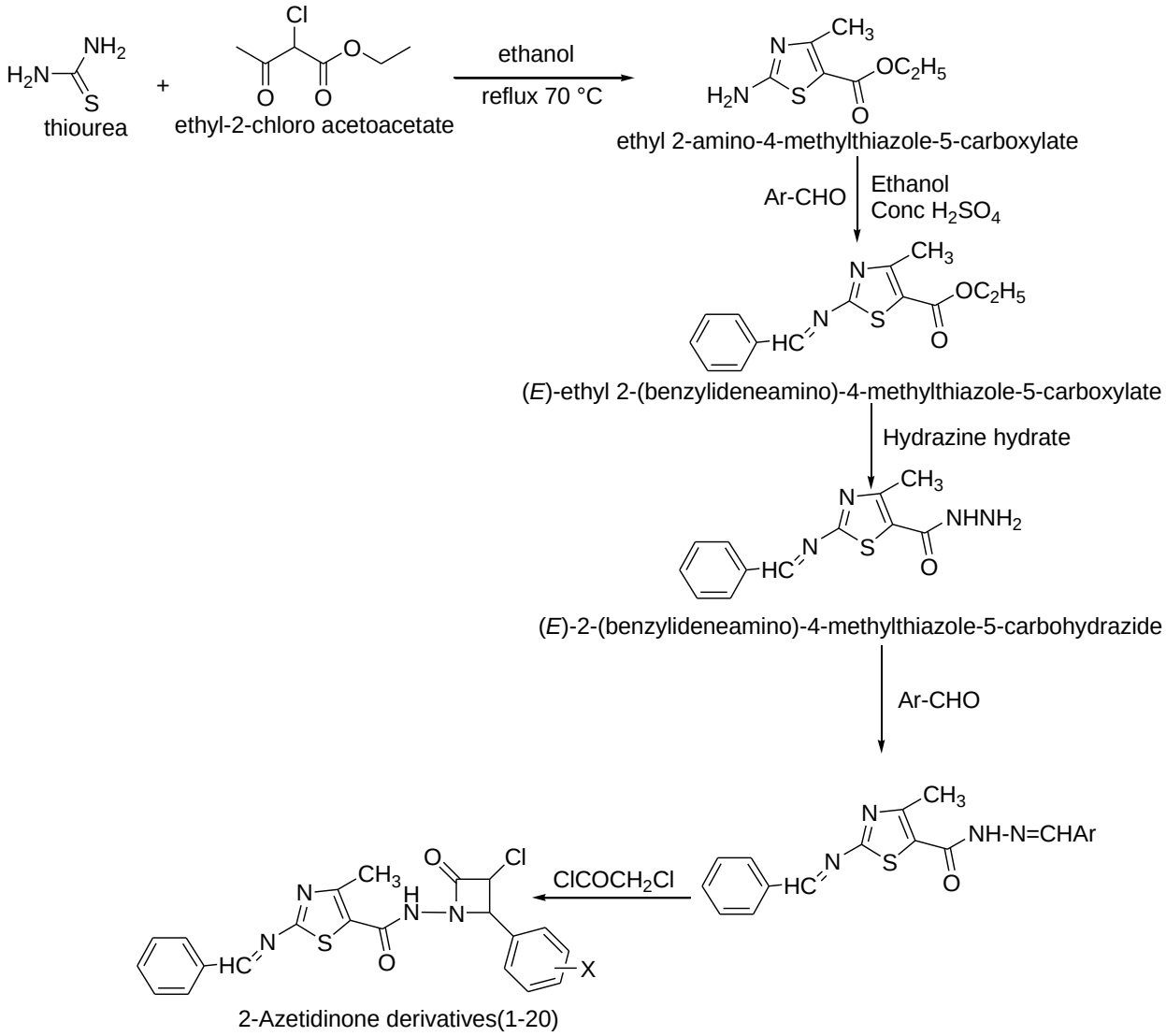

Table-1 Physical data of 2-azetidinone derivatives

Comp.	M. Formula	X	M. Pt. (°C)	M. Wt.	R_f value*	% yield
1	**$C_{24}H_{23}ClN_4O_5S$**	3,4,5-methoxy benzaldehyde	187-189	**514.98**	0.68	77
2	**$C_{22}H_{19}ClN_4O_3S$**	3-methoxy benzaldehyde	167-170	**454.93**	0.59	66
3	**$C_{21}H_{17}ClN_4O_3S$**	2-hydroxy benzaldehyde	201-203	**440.9**	0.76	82
4	**$C_{21}H_{16}ClN_5O_4S$**	3-nitro benzaldehyde	175-177	**469.9**	0.67	73

5	**$C_{21}H_{16}C_{l2}N_4O_2S$**	3-chloro benzaldehyde	193-195	**459.35**	0.70	76
6	**$C_{22}H_{19}ClN_4O_2S$**	4-methyl benzaldehyde	190-191	**438.93**	0.67	69
7	**$C_{21}H_{16}BrClN_4O_2S$**	4-bromo benzaldehyde	200-202	**503.8**	0.66	85
8	**$C_{23}H_{22}ClN_5O_2S$**	4-dimethyl amino benzaldehyde	185-187	**467.97**	0.77	64
9	**$C_{21}H_{16}ClN_5O_4S$**	4-nitro benzaldehyde	170-172	**469.9**	0.69	77
10	**$C_{21}H_{16}ClFN_4O_2S$**	4-fluorobenzaldehyde	273-275	**442.89**	0.64	68
11	**$C_{21}H_{16}Cl_2N_4O_2S$**	4-chloro benzaldehyde	177-179	**459.35**	0.64	70
12	**$C_{25}H_{26}ClN_5O_2S$**	4-diethylamino benzaldehyde	181-183	**496.02**	0.72	73
13	**$C_{22}H_{19}ClN_4O_4S$**	4-hydroxy-3-methoxy benzaldehyde	195-197	**470.93**	0.58	66
14	**$C_{21}H_{16}ClFN_4O_2S$**	3-fluorobenzaldehyde	265-267	**442.89**	0.67	72
15	**$C_{22}H_{19}ClN_4O_3S$**	2-methoxy benzaldehyde	167-169	**454.93**	0.83	63
16	**$C_{21}H_{15}Cl_3N_4O_2S$**	2,4-dichloro benzaldehyde	237-239	**493.79**	0.65	83
17	**$C_{21}H_{16}BrClN_4O_2S$**	3-bromo benzaldehyde	211-213	**503.8**	0.75	74
1 8	**$C_{21}H_{17}ClN_4O_2S$**	Benzaldehyde	169-171	**424.9**	0.63	74
19	**$C_{21}H_{16}Cl_2N_4O_2S$**	2-chloro benzaldehyde	189-191	**459.35**	0.68	81
20	**$C_{21}H_{16}BrClN_4O_2S$**	2-bromo benzaldehyde	145-147	**503.8**	0.70	80

Solvent: Benzene

Spectral data:

(E)-2-(benzylideneamino)-N-(3-chloro-2-oxo-4-(3,4,5-trimethoxyphenyl)azetidin-1-yl)-4-methylthiazole-5-carboxamide (1) IR (KBr, cm^{-1}): 3472(NH), 3010 (C-H Ar), 2880 (C-H str., -CH_3), 1722 (C=O), 1638 (C=N str), 1603 (C=C Ar), 1366 (C-N), 1248(C–O–C str), 761(C–Cl), 747(C-S); ^{1}H NMR (DMSO-*d*6, 400 MHz): 8.66-7.23 (m, 7H, ArH), 7.20(s, 1H, CH=N), 3.89 (s, 1H, CH azetidinone), 3.29 (s, 9H, –OCH_3), 2.49 (s, 1H, CH_3 thiazole).

(E)-2-(benzylideneamino)-N-(3-chloro-2-(3-methoxyphenyl)-4-oxoazetidin-1-yl)-4-methylthiazole-5-carboxamide (2) IR (KBr, cm^{-1}): 3587(NH), 3005 (C-H Ar), 2877 (C-H str., -CH_3), 1633 (C=N str), 1610 (C=C Ar), 1346 (C-N), 1259(C–O–C str), 783(C–Cl), 747(C-S); ^{1}H NMR (DMSO-*d*6, 400 MHz): 8.35-7.59 (m, 9H, ArH), 7.03(s, 1H, CH=N), 3.89 (s, 1H, CH azetidinone), 3.31 (s, 3H, –OCH_3), 2.50 (s, 1H, CH_3 thiazole).

(E)-2-(benzylideneamino)-N-(3-chloro-2-(2-hydroxyphenyl)-4-oxoazetidin-1-yl)-4-methylthiazole-5-carboxamide (3) IR (KBr, cm^{-1}): 3607(OH), 3564(NH), 3008 (C-H Ar), 2946 (C-H str., -CH_3), 1706 (C=O), 1644 (C=N str), 1626 (C=C Ar), 1373 (C-N), 792(C–Cl), 744(C-S); ^{1}H NMR (DMSO-*d*6, 400 MHz): 8.48-7.59 (m, 9H, ArH), 7.56(s, 1H, CH=N), 3.43 (s, 1H, CH azetidinone), 2.50 (s, 1H, CH_3 thiazole).

(E)-2-(benzylideneamino)-N-(3-chloro-2-(3-nitrophenyl)-4-oxoazetidin-1-yl)-4-methylthiazole-5-carboxamide (4) IR (KBr, cm^{-1}): 3430(NH), 3013 (C-H Ar), 2908 (C-H str., -CH_3), 1689 (C=O), 1628 (C=N str), 1605 (C=C Ar), 1525 (N–O str, NO2), 1346 (C-N), 763(C–Cl), 713(C-S); ^{1}H NMR (DMSO-*d*6, 400 MHz): 8.60-7.47 (m, 9H, ArH), 7.12(s, 1H, CH=N), 3.31 (s, 1H, CH azetidinone), 2.50 (s, 1H, CH_3 thiazole).

(E)-2-(benzylideneamino)-N-(3-chloro-2-(3-chlorophenyl)-4-oxoazetidin-1-yl)-4-methylthiazole-5-carboxamide (5) IR (KBr, cm^{-1}): 3444(NH), 3071 (C-H Ar), 2913 (C-H str., -CH_3), 1705 (C=O), 1628 (C=N str), 1595 (C=C Ar), 1384 (C-N), 743(C–Cl), 713(C-S); ^{1}H NMR (DMSO-*d*6, 400 MHz): 8.57-7.51 (m, 9H, ArH), 7.22(s, 1H, CH=N), 3.82 (s, 1H, CH azetidinone), 2.50 (s, 1H, CH_3 thiazole).

(E)-2-(benzylideneamino)-N-(3-chloro-2-oxo-4-p-tolylazetidin-1-yl)-4-methylthiazole-5-carboxamide (6) IR (KBr, cm^{-1}): 3313(NH), 2957 (C-H Ar), 2899 (C-H str., -CH_3), 1701 (C=O), 1677 (C=N str), 1635 (C=C Ar), 1396(C-N), 749(C–Cl), 735(C-S); ^{1}H NMR (DMSO-*d*6, 400 MHz): 7.96-7.33 (m, 9H, ArH), 7.25(s, 1H, CH=N), 3.41 (s, 1H, CH azetidinone), 3.16 (s, 3H, –CH_3), 2.49(s, 1H, CH_3 thiazole).

(E)-2-(benzylideneamino)-N-(2-(4-bromophenyl)-3-chloro-4-oxoazetidin-1-yl)-4-methylthiazole-5-carboxamide (7) IR (KBr, cm^{-1}): 3325(NH), 3053 (C-H Ar), 2961 (C-H str., -CH_3), 1636 (C=N str), 1599 (C=C Ar), 1351 (C-N), 771(C–Cl), 739(C-S), 649 (Br); ^{1}H NMR (DMSO-*d*6, 400 MHz): 8.89-7.16 (m, 9H, ArH), 7.14(s, 1H, CH=N), 3.31 (s, 1H, CH azetidinone), 2.49 (s, 1H, CH_3 thiazole).

(E)-2-(benzylideneamino)-N-(3-chloro-2-(4-(dimethylamino)phenyl)-4-oxoazetidin-1-yl)-4-methylthiazole-5-carboxamide (8) IR (KBr, cm^{-1}): 3402(NH), 3004 (C-H Ar), 2888 (C-H str., -CH_3), 1685 (C=O), 1634 (C=N str), 1609 (C=C Ar), 1378(C-N), 778(C–Cl), 737(C-S); ^{1}H NMR (DMSO-*d*6, 400 MHz): 7.89-7.13 (m, 9H, ArH), 7.12(s, 1H, CH=N), 3.88 (s, 1H, CH azetidinone), 2.50 (s, 1H, CH_3 thiazole), 2.07 (s, 6H, N $(CH3)_2$).

(E)-2-(benzylideneamino)-N-(3-chloro-2-(4-nitrophenyl)-4-oxoazetidin-1-yl)-4-methylthiazole-5-carboxamide (9) IR (KBr, cm^{-1}): 3379(NH), 3067 (C-H Ar), 2938 (C-H str., -CH_3), 1672 (C=O), 1638 (C=N str), 1602 (C=C Ar), 1548 (N–O str, NO2), 1378 (C-N), 772(C–Cl), 743(C-S); ^{1}H NMR (DMSO-*d*6, 400 MHz): 7.94-7.33 (m, 9H, ArH), 7.00(s, 1H, CH=N), 3.88 (s, 1H, CH azetidinone), 2.50 (s, 1H, CH_3 thiazole).

(E)-2-(benzylideneamino)-N-(3-chloro-2-(4-fluorophenyl)-4-oxoazetidin-1-yl)-4-methylthiazole-5-carboxamide (10) IR (KBr, cm^{-1}): 3473(NH), 3024 (C-H Ar), 2938 (C-H str., -CH_3), 1689 (C=O), 1634 (C=N str), 1544 (C=C Ar), 1352 (C-N), 1258 (C–F), 784(C–Cl), 707(C-S); ^{1}H NMR (DMSO-*d*6, 400 MHz): 8.27-7.43 (m, 9H, ArH), 7.21(s, 1H, CH=N), 3.86 (s, 1H, CH azetidinone), 2.50 (s, 1H, CH_3 thiazole).

(E)-2-(benzylideneamino)-N-(3-chloro-2-(4-chlorophenyl)-4-oxoazetidin-1-yl)-4-methylthiazole-5-carboxamide (11) IR (KBr, cm^{-1}): 3419(NH), 3011 (C-H Ar), 2971 (C-H str., -CH_3), 1672 (C=O), 1634 (C=N str), 1602 (C=C Ar), 1368 (C-N), 733(C–Cl), 686(C-S); ^{1}H NMR (DMSO-*d*6, 400 MHz): 7.63-7.29 (m, 9H, ArH), 7.22(s, 1H, CH=N), 3.80 (s, 1H, CH azetidinone), 2.90 (s, 1H, CH_3 thiazole).

(E)-2-(benzylideneamino)-N-(3-chloro-2-(4-(diethylamino)phenyl)-4-oxoazetidin-1-yl)-4-methylthiazole-5-carboxamide(12) IR (KBr, cm^{-1}): 3307(NH), 3079 (C-H Ar), 2989 (C-H str., -CH_3), 1641 (C=N str), 1578 (C=C Ar), 1324 (C-N), 774(C–Cl), 714(C-S); ^{1}H NMR (DMSO-*d*6, 400 MHz): 8.99-7.51 (m, 9H, ArH), 7.22(s, 1H, CH=N), 3.31(m, 6H, CH_3), 2.50(m, 4H, CH_2).

(E)-2-(benzylideneamino)-N-(3-chloro-2-(4-hydroxy-3-methoxyphenyl)-4-oxoazetidin-1-yl)-4-methylthiazole-5-carboxamide(13) IR (KBr, cm^{-1}):3488 (OH) 3388(NH), 3030 (C-H Ar), 2898 (C-H str., -CH_3), 1602 (C=N str), 16506 (C=C Ar), 1387 (C-N), 1249(C–O–C str), 777(C–Cl), 744(C-S); ^{1}H NMR (DMSO-*d*6, 400 MHz): 9.13-7.83 (m, 8H, ArH), 7.32(s, 1H, CH=N), 3.88 (s, 1H, CH azetidinone), 3.39 (s, 3H, –OCH_3), 2.49 (s, 1H, CH_3 thiazole).

(E)-2-(benzylideneamino)-N-(3-chloro-2-(3-fluorophenyl)-4-oxoazetidin-1-yl)-4-methylthiazole-5-carboxamide (14) IR (KBr, cm^{-1}): 3341(NH), 3051 (C-H Ar), 2944 (C-H str., -CH_3), 1681 (C=O), 1632 (C=N str), 1603 (C=C Ar), 1348 (C-N), 1288 (C–F), 747(C–Cl), 695(C-S); ^{1}H NMR (DMSO-*d*6, 400 MHz): 8.13-7.283 (m, 9H, ArH), 6.97(s, 1H, CH=N), 3.60 (s, 1H, CH azetidinone), 2.50 (s, 1H, CH_3 thiazole).

(E)-2-(benzylideneamino)-N-(3-chloro-2-(2-methoxyphenyl)-4-oxoazetidin-1-yl)-4-methylthiazole-5-carboxamide (15) IR (KBr, cm^{-1}): 3428(NH), 3026 (C-H Ar), 2963 (C-H str., -CH_3), 1685 (C=O), 1633 (C=N str), 1604 (C=C Ar), 1346 (C-N), 1259(C–O–C str), 785(C–Cl), 718(C-S); ^{1}H NMR (DMSO-*d*6, 400 MHz): 8.52-7.11 (m, 9H, ArH), 7.01(s, 1H, CH=N), 3.75 (s, 1H, CH azetidinone), 3.33 (s, 3H, –OCH_3), 2.42 (s, 1H, CH_3 thiazole).

(E)-2-(benzylideneamino)-N-(3-chloro-2-(2,4-dichlorophenyl)-4-oxoazetidin-1-yl)-4-methylthiazole-5-carboxamide(16) IR (KBr, cm^{-1}): 3431(NH), 3002 (C-H Ar), 2886 (C-H str., -CH_3), 1711 (C=O), 1659 (C=N str), 1559 (C=C Ar), 1348 (C-N), 715(C–Cl), 681(C-S); ^{1}H NMR (DMSO-*d*6, 400 MHz): 8.16-7.12 (m, 8H, ArH), 6.75(s, 1H, CH=N), 3.43 (s, 1H, CH azetidinone), 2.49 (s, 1H, CH_3 thiazole).

(E)-2-(benzylideneamino)-N-(2-(3-bromophenyl)-3-chloro-4-oxoazetidin-1-yl)-4-methylthiazole-5-carboxamide (17) IR (KBr, cm^{-1}): 3437(NH), 3049 (C-H Ar), 2901 (C-H str., -CH_3), 1595 (C=N str), 1296 (C-N), 775(C–Cl), 730(C-S), 682 (Br); ^{1}H NMR (DMSO-*d*6, 400 MHz): 8.44-7.74 (m, 9H, ArH), 7.47(s, 1H, CH=N), 4.12 (s, 1H, CH azetidinone), 2.50 (s, 1H, CH_3 thiazole).

(E)-2-(benzylideneamino)-N-(3-chloro-2-oxo-4-phenylazetidin-1-yl)-4-methylthiazole-5-carboxamide(18) IR (KBr, cm^{-1}): 3335(NH), 2980 (C-H Ar), 2895 (C-H str., -CH_3), 1659 (C=O), 1620 (C=N str), 1575 (C=C Ar), 1339 (C-N), 749(C–Cl), 680(C-S); ^{1}H NMR (DMSO-*d*6, 400 MHz): 9.97-7.93 (m, 10H, ArH), 7.27(s, 1H, CH=N), 3.32 (s, 1H, CH azetidinone), 2.50 (s, 1H, CH_3 thiazole).

(E)-2-(benzylideneamino)-N-(3-chloro-2-(2-chlorophenyl)-4-oxoazetidin-1-yl)-4-methylthiazole-5-carboxamide(19) IR (KBr, cm^{-1}): 3561(NH), 3006 (C-H Ar), 2897 (C-H str., -CH_3), 1714 (C=O), 1662 (C=N str), 1617 (C=C Ar), 1347 (C-N), 786(C–Cl), 702(C-S); ^{1}H NMR (DMSO-*d*6, 400 MHz): 8.92-7.63 (m, 9H, ArH), 7.13(s, 1H, CH=N), 3.88 (s, 1H, CH azetidinone), 2.50 (s, 1H, CH_3 thiazole).

(E)-2-(benzylideneamino)-N-(2-(2-bromophenyl)-3-chloro-4-oxoazetidin-1-yl)-4-methylthiazole-5-carboxamide(20) IR (KBr, cm^{-1}): 3549(NH), 3146 (C-H Ar), 2973 (C-H str., -CH_3), 1700 (C=O), 1650 (C=N str), 1614 (C=C Ar), 1332 (C-N), 753(C–Cl), 732(C-S), 683 (Br) ; ^{1}H NMR (DMSO-*d*6, 400 MHz): 8.55-7.56 (m, 9H, ArH), 6.77(s, 1H, CH=N), 3.31 (s, 1H, CH azetidinone), 2.49 (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[16] 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[17].

Evaluation of anticancer activity

The anticancer activity of synthesized compounds (**1-20**) 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 [17].

Table 2. *In Vitro* Antimicrobial Activity of the Title Compounds (**1-20)**

Compound	Minimum inhibitory concentration (µg ml^{-1})				
	Bacterial Strains			Fungal Strains	
	E. coli	*S. aureus*	*B. subtilis*	*C. albicans*	A. *Niger*
1	12.5	12.5	25	12.5	25
2	12.5	25	50	12.5	12.5
3	12.5	6.25	6.25	12.5	12.5
4	**1.56**	**3.12**	**1.56**	12.5	12.5
5	25	25	12.5	**3.12**	**1.56**
6	12.5	25	25	12.5	25
7	12.5	25	12.5	50	12.5
8	25	12.5	6.25	12.5	12.5
9	12.5	25	12.5	50	12.5
10	25	12.5	25	25	25
11	**1.56**	12.5	**1.56**	50	25
12	25	25	25	25	25
13	25	12.5	25	12.5	**1.56**
14	12.5	25	12.5	50	25
15	6.25	12.5	12.5	25	25
16	25	25	25	25	12.5
17	12.5	25	12.5	50	25
18	6.25	12.5	12.5	25	25
19	25	25	25	6.25	25
20	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 3. Anticancer Activity of the Title Compounds (**1-20)**

S. No.	**Compound**	**IC_{50}(µM)**
1	1	88.80
2	2	234.12
3	3	59.07
4	4	354.69
5	5	512.65
6	6	132.87
7	7	168.32
8	8	94.36
9	9	**58.86**
10	10	103.75
11	11	95.08
12	12	110.24
13	13	167.89
14	14	357.67
15	15	75.98
16	16	163.95
17	17	372.09
18	18	76.12
19	19	125.56
20	20	178.56
STD Drug	Doxorubicin	16.12±0.682

Result and Discussion:

Antimicrobial activity results (Table 2) indicated that the synthesized compounds were having good antimicrobial activity but was less active as compared to standard drugs. Compound **4** and compound **11** was found to be most effective against bacterial strains (MIC= 1.56 µg/ml against E. coli and *B. subtilis*) and compound 4 (MIC= 3.12 µg/ml) against *S. aureus*. Compound **5** and compound **13** (MIC = 1.56 µg/ml for A. *Niger and* MIC = 3.12 µg/ml for C. albicans) was found to be most potent antifungal agent. In general, compound **4** was found to be most potent antimicrobial agent among the synthesized derivatives but less active as compared to the standard drug.

Anticancer activity results (Table 2) indicated that the synthesized compounds exhibited weak anticancer activity against Hela cancer cell line as compared to standard drug. Compound 9 (IC_{50} = **58.86 µM**) was found to be most potent anticancer agent.

Conclusion

In the present study, a series of 2-azetidinone derivatives (1 – 20) was synthesized and evaluated for their in vitro antimicrobial and anticancer potentials. The synthesized compounds exhibit more potent antimicrobial activity as compared to their anticancer activity. Compound 4 was found to be most potent antimicrobial agent. In case of anticancer activity, compound 9 (IC_{50} = **58.86 µM**) was found to be most potent anticancer agent.

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