Available online at www.derpharmachemica.com

ISSN 0975-413X
CODEN (USA): PCHHAX

Der Pharma Chemica, 2017, 9(20):10-15
(http://www.derpharmachemica.com/archive.html)

Discovery of Clubbed Thiazolo [3,2-a]pyrimidinones as Antimicrobial Agents

Babasaheb Zine[1], Sunil Jadhav[2], Prashant Dixit[3], Mazahar Farooqui[2,4*]

[1]Department of Chemistry, Bhagwan Mahavidyalaya, Ashti, Dist. Beed-414203, Maharashtra, India
[2]Post Graduate and Research Center, Maulana Azad College, Aurangabad-431001, Maharashtra, India
[3]Dr. Babasaheb Ambedkar Marathawada University, Subcampus, Osmanabad-413501, Maharashtra, India
[4]Dr. Rafiq Zakaria College for Women, Aurangabad- 431001, Maharashtra, India

ABSTRACT

Bacterial and fungal infections represent one of the most prevalent health problems that cause functional disability, leading to lifestyle sacrifice and further complications. Upcoming needs for the clinical drugs candidates for the improvement signifies an exciting and challenging approach to improve the clinical efficacy of current drugs in the development of new therapeutic approaches. Current report reveals the synthesis of fused pyrimidinones and their evaluation against above antibacterial and antifungal therapeutic area. Out of 12 compounds reported here, many of them displayed decent antibacterial and antifungal profiles. We report herewith most prominent molecules 5d, 5e, 5f, 5g, 5h and 5i. In conclusion, 5g have been identified as the lead with the most prominent results.

Keywords: Pyrimidinones, Therapeutic, Antibacterial, Antifungal

INTRODUCTION

Fungal infections can be considered as serious medical issue now days because of substantial increase in the numbers of patients exposed for the organs transplants, clinical treatments for AIDS and anticancer chemotherapy. Marketed drugs like fluconazole, miconazoles etc. obeys good activity spectrum [1]. These azole antifungal inhibit the cytochrome 450 dependent enzyme lanosterol 14-alpha-demethylase, which converts lanosterol to ergosterol, the key sterol in fungal cell membrane. Depletion of ergosterol damages the cell membranes resulting in the cell death. However the continuous clinical use of these azoles results in the emergence of drug resistance [2-4] leads to upcoming need. The emergence of resistance in antibacterial therapy is severe health issue on mankind across globe. The bacterial infections like tuberculosis, the infection on the boarder of eradications once, continues to be major cause for the death lately. To tackle bacterial resistance, there is a humble clinical need for new antibacterial agents with improved activity.

Electron-rich nitrogen heterocycles and sulfur having compounds play a significant function in various biological activities. Thiazolo [3,2-*a*] pyrimidinone nucleus have been constantly regarded as structural similarities like biogenic purine bases and can be considered as potential purine antagonists [5]. These heterocyclic compounds are the key chemical building blocks for numerous compounds that also play important roles in the functioning of biologically active molecules. As one type of those heterocyclic rings, 5*H*-thiazolo [3,2-*a*]pyrimidin-5-ones are considered a promising class of bioactive heterocyclic compound having a wide range of biological activities such as anti-inflammatory [6,7], antihypertensis [6-8], antifungal [9], antibiofilm [10] activity. These compounds also shows antibacterial [11], antiviral [12], antioxidant [13], antitumor [14,15], anti-HIV [16], calcium channel blocking [17], antitubercular [18] activity. Most of the studies have also suggested amino and mercapto position's availability for extensive variation for modulation of activity. Thus to impart better anti-bacterial activity, we linked thiazolol[3,2-*a*] pyrimidinones nucleus to the hybrid (combination) design. Target structure was combination of two precursors viz., protected thiazolo[3,2-a] pyrimidinones and a chromone moiety fused with multi-substituted phenyl ring.

MATERIALS AND METHODS

The melting points of the synthesized compound were determined in open capillary tubes and uncorrected. The ^{1}H-NMR and for the compound synthesized were recorded (DMSO-d_6) on a Varian (400 MHz) using TMS as an internal standard. Chemical values are given δ scales. The spectra of mass were recorded on ES-MS. The completion of reactions was monitored by Thin Layer Chromatography (TLC) on silica gel coated aluminium sheets. The spots were visualized by UV light. Necessary chemicals were ordered from Sigma-Aldrich and Spectrochim (INDIA). Commercial grade solvents were used without further purification.

Synthetic methodology

General procedure for the synthesis of substituted acetic acid-2-acetyl phenyl ester intermediate (1)

To a stirred solution (clear and transparent solution) of substituted 2-hydroxy acetophenone (1.0 mol) in pyridine (10 volumes) at 5°C, acetyl chloride (1.2 mol) was added in single lot. Cooling was removed and suspension was stirred for overnight at room temperature. White colour solid product was collected after filtration and pyridine washing.

General procedure for the synthesis of substituted 1-(2-hydroxy-phenyl)-butane-1, 3-dione (2)

The product obtain in step 1 (1.0 mol) was dissolved in 10 volume ethanol, to that around 2.5 volume water was added and stirred for 5 min. Powdered KOH (2.5 mol) was added and reaction was stirred for overnight at room environment. On a next day pH of white suspension was adjusted up to 4-4.5 using concentrated HCl. Product was filtered and washed by ethanol in decent yield (75-80%). Crude product was crystallized by heating in ethanol; reaction conversion was monitored by TLC.

General procedure for the synthesis of substituted 4-oxo-4H-chromene-2-carbaldehyde (3)

Crystallized product from step 2 was dissolved in Dimethylsulphoxide (DMSO) (10 volumes) and to that a solid of catalytic amount of DMSO was added. Reaction was stirred for 4-5 h. at 78-80°C. Conversion was monitored by TLC. After reaction completion, water (10 volumes) was added, reaction mass was washed by ethyl acetate (2 × 5 volumes). Ethyl acetate was removed to obtain crude mass. It was then dissolved in ethanol, heated it 80°C. This clear transparent solution was then cooled and product was collected after filtration and ethanol washing in moderate to good yields (40-60%).

General procedure for synthesis of 5-oxo-5H-[1, 3]thiazolo [3,2-a]pyrimidin-7-yl methyl triphenyl phosphonium chloride (Wittig reagent) (4)

To a stirred suspension of 7-(chloromethyl)-5H-thiazolo[3,2-a]pyrimidin-5-one (0.029 mol) (1) in acetonitrile was added triphenylphosphine (0.032 mol) (2) at room temperature. The resulting reaction mixture was slowly heated to reflux for 30 min. The solvent was concentrated in vacuo and the residue stirred with di-isopropyl ethyl ether and filtered. The solid was dried under vacuum to afford the desired compound as an off-white solid (3), 79%. M.p.: 158-160°C. ^{1}H-NMR (400 MHz, DMSO-d_6): δ=4.86 (d, J=15.0 Hz, 2H), 6.45 (br. s, 1H), 7.32 (br. s, 1H), 7.60 - 7.74 (m, 15H), 7.86 (br. s, 1H); MS (m/z): 463 $[M+H]^+$.

General procedure for preparation of substituted chromone thiazolo pyrimidinone (5a-l)

NaH (2 mol) was added to previously stirred solution of thizolol triphenyl phosphonium chloride salt (3) (1 mol) in Dimethylformamide (DMF) (5 volumes) at 0-5°C carefully within 4-5 portion. This reaction mixture was stirred for 30 min at same temperature. Then substituted chromone-2-carbaldehyde (from step 3, 2 mol) was added slowly and stirred it for about 4-6 h at room temperature. Completion of reaction checked by TLC. Reaction mixture was poured into ice water. Stirred and then the targeted product 5(a-l) obtained was filtered. Washed by water and crude product was crystallized using ethanol (Yields 65-87%). Their structures have been confirmed by Mass, IR and ^{1}H-NMR spectra.

(E)-7-(2-(6-chloro-3-fluoro-4-oxo-4H-chromen-2-ylvinyl)-5H-thiazolo [3,2-a] pyrimidin-5-one (5a): Pale yellow solid; Yield: 70%; M.p.: 142-144°C; IR (KBr, cm^{-1}) 1678 (C=O), 3082 (Ar-H), 1620 and 1562 (C=C), 1466 (C=N), 1327 (C-S), ^{1}H-NMR (400 MHz, DMSO-d_6), δ=6.97 (d, 1H, Thiazole H), 7.69 (d, 1H, Thiazole H), 7.37 (s, 1H, Ar-H), 7.42 and 7.45 (d, 2H, olefinic H), 8.02 (d, 1H, Ar-H), 8.18 (d, 1H, Ar-H), 8.4 (s, 1H, Pyrimidinone H). MS (m/z): 375 $[M+H]^+$.

(E)-7-(2-(6-chloro-3-fluoro-7-methyl-4-oxo-4H-chromen-2-yl) vinyl) -5H – thiazolo [3,2-a]pyrimidin-5-one (5b): Faint yellow solid; Yield: 78%; M.p: 158-160°C; IR: (KBr, cm^{-1}): 1678 (C=O), 3035 (Ar-H), 1636 and 1595 (C=C), 1473 (C=N), 1338 (C-S); ^{1}H-NMR (400 MHz, DMSO-d_6), δ=2.32 (s, 3H, CH_3 H), 6.93 (s, 1H, Ar-H), 7.36 and 7.43 (s, 2H, olef. H), 7.7 (d, 1H, Thiazole H), 8.46 (s, 1H, Ar-H), 8.17(d, 1H, Thiazole H), 8.02(s, 1H, Pyrimidinone H); MS (m/z): 388 $[M+H]^+$.

(E)-7-(2-(6-Bromo-3-fluoro-4-oxo-4H-chromen-2-yl)vinyl)-5H-thiazolo[3,2-a] pyrimidin-5-one (5c): Yellow solid; Yield: 87%; M.p.: 181-183°C; IR (KBr, cm^{-1}) 1689 (C=O), 3052 (Ar-H), 1634 and 1569(C=C), 1446 (C=N), 1356 (C-S); ^{1}H-NMR (400 MHz, DMSO-d_6), δ=6.65 (d, 1H, Thiazole H), 7.56 (d, 1H, Thiazole H), 7.52 (s, 1H, Ar-H), 7.45 and 7.48 (d, 2H, olefinic), 8.12 (d, 1H, Ar-H), 8.21 (d, 1H, Ar-H), 8.2 (s, 1H, Pyrimidinone H); MS (m/z): 420$[M+H]^+$.

(E)-7-(2-(6-Iodo-3-fluoro-4-oxo-4H-chromen-2-yl)vinyl)-5H-thiazolo[3,2-a]pyrimidin-5-one (5d): Buff white solid; Yield: 76%; M.p.: 194-196°C; IR (KBr, cm^{-1}): 1656 (C=O), 3077 (Ar-H), 1628 and 1568 (C=C), 1486 (C=N), 1387 (C-S); ^{1}H-NMR: (400 MHz, DMSO-d_6) 6.65 (d, 1H, Thiazole H), 7.76 (d, 1H, Thiazole H), 7.44 (s, 1H, Ar-H), 7.34 and 7.37 (d, 2H, olefinic), 8.21 (d, 1H), 8.32 (d, 1H), 8.12 (s, 1H, Pyrimidinone H); MS (m/z): 467 $[M+H]^+$.

(E)-7-(2-(7-methyl-4-oxo-4H-chromen-2-yl)vinyl)-5H-thiazolo[3,2-a]pyrimidin-5-one (5e): Light yellow solid; Yield: 83%; M.p.: 154-156°C; IR (KBr, cm^{-1}), 3078 (Ar-H), 1674 (C=O); 1643 and 1546 (C=C), 1477 (C=N), 1342 (C-S); ^{1}H-NMR (400 MHz, DMSO-d_6), δ=2.40 (s, 3H, CH_3), 6.87 (d, 1H, Thiazole H), 7.1 (d, 1H, Thiazole H), 7.26 (d, 1H, Ar-H), 7.15 (s, 1H, Ar-H), 7.49 and 7.50 (d, 2H olefinic), 7.91 (s, 1H, Ar-H), 8.17 (s, 1H, Pyrimidinone H), 7.97 (s, 1H, pyranone-H); MS (m/z): 337 $[M+H]^+$.

(E)-7-(2-(6-chloro-7-methyl-4-oxo-4H-chromen-2-yl)vinyl)-5H-thiazolo[3,2-a]pyrimidin-5-one (5f): Faint yellow solid; Yield: 89%; M.p.: 134-136°C; IR (KBr, cm^{-1}) 1687 (C=O), 3065 (Ar-H), 1660 and 1545 (C=C), 1443 (C=N), 1368 (C-S); ^{1}H-NMR (400 MHz, DMSO-d_6), δ=2.41 (s, 3H, CH_3), 6.93 (s, 1H, Ar-H), 7.21 and 7.32 (d, 2H, olef. H), 7.65 (d, 1H, Thiazole H), 8.36 (s, 1H, Ar-H), 8.43 (d, 1H, Thiazole H), 8.0 (s, 1H, Pyrimidinone H), 7.8 (s, 1H, pyranone-H); MS (m/z): 371 $[M+H]^+$.

(E)-7-(2-(6-bromo-3-fluoro-7-methyl-4-oxo-4H-chromen-2-yl)vinyl)-5H-thiazolo[3,2-a]pyrimidin-5-one (5g): Faint brown solid; Yield: 79%; M.p.: 172-174°C; IR (KBr, cm^{-1}), 1697 (C=O), 3045 (Ar-H), 1613 and 1588 (C=C), 1467 (C=N), 1387 (C-S); ^{1}H-NMR, (400 MHz, DMSO-d_6), δ=2.22 (s, 3H, CH_3), 6.67 (s, 1H, Ar-H), 7.3 and 7.35 (d, 2H, olefinic H), 7.4 (d, 1H, Thiazole H), 8.26 (s, 1H, Ar-H), 8.17 (d, 1H, Thiazole H), 8.11 (s, 1H, Pyrimidinone H); MS (m/z): 434 $[M+H]^+$.

(E)-7-(2-(6-Iodo-3-fluoro-7-methyl-4-oxo-4H-chromen-2-yl)vinyl)-5H-thiazolo[3,2-a]pyrimidin-5-one (5h): Yellow solid; Yield: 78%; M.p.: 190-192°C; IR (KBr, cm^{-1}), 1671 (C=O), 3065 (Ar-H), 1623 and 1595 (C=C), 1476 (C=N), 1378 (C-S). ^{1}H-NMR, (400 MHz, DMSO-d_6), δ=2.45 (s, 3H, CH_3), 6.73 (s, 1H, Ar-H), 7.5 and 7.55 (d, 2H, olefinic H), 7.7 (d, 1H, Thiazole H), 8.26 (s, 1H, Ar-H), 8.47 (d, 1H, Thiazole H), 8.52 (s, 1H, Pyrimidinone H) MS (m/z): 481 $[M+H]^+$.

(E)-7-(2-(5,7-dichloro-4-oxo-4H-chromen-2-yl)vinyl)-5H-thiazolo[3,2-a]pyrimidin-5-one (5i): Faint yellow solid; Yield: 78%; M.p.: 147-149°C; IR (KBr, cm^{-1}), 1678 (C=O), 3035 (Ar-H), 1636 and 1595 (C=C), 1473 (C=N), 1338 (C-S); ^{1}H-NMR, (400 MHz, DMSO-d_6), δ=6.93 (d, 1H, Thiazole H), 8.08 (d, 1H, Thiazole H), 7.32 and 7.4 (d, 2H, olefinic H), 7.7 (s, 1H), 8.46 (s, 1H), 8.17 (s, 1H, Pyrimidinone H), 7.91 (s, 1H, pyranone-H); MS (m/z): 392 $[M+H]^+$.

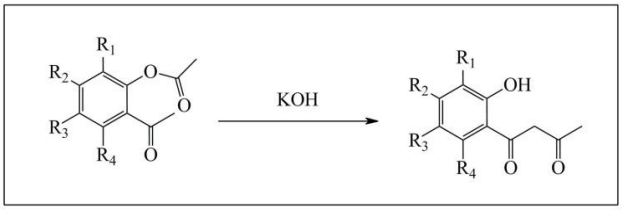
(E)-7-(2-(5,7-dimethyl-4-oxo-4H-chromen-2-yl)vinyl)-5H-thiazolo[3,2-a]pyrimidin-5-one (5j): Faint brown solid; Yield: 68%; M.p.: 203-205°C; IR (KBr, cm^{-1}), 1688 (C=O), 3056 (Ar-H), 1613 and 1595 (C=C), 1446 (C=N), 1342 (C-S); ^{1}H-NMR (400 MHz, DMSO-d_6), δ=2.22 (s, 3H CH_3), 2.38 (s, 3H, CH_3), 6.26 (d, 1H, Thiazole H), 6.93 (s, 1H, Ar-H), 7.23 and 7.35 (d, 2H, olefinic H), 7.7 (s, 1H, Ar-H), 8.46 (s, 1H, pyranone-H), 8.17 (d, 1H, Thiazole H), 8.18 (s, 1H, Pyrimidinone H); MS (m/z): 350 $[M+H]^+$.

(E)-7-(2-(7-methoxy-4-oxo-4H-chromen-2-yl)vinyl)-5H-thiazolo[3,2-a]pyrimidin-5-one (5k): White solid; Yield: 65%; M.p.: 181-183°C; IR (KBr, cm^{-1}), 1677 (C=O), 2098 (Ar-H), 1623 and 1556 (C=C), 1444 (C=N), 1376 (C-S); ^{1}H-NMR, (400 MHz, DMSO-d_6), δ=3.47 (s, 3H, OCH_3), 6.93 (s, 1H, Ar-H), 6.33 (d, 1H, Thiazole H), 7.45 and 7.49 (d, 2H, olefinic H), 7.74 (d, 1H, Thiazole H), 8.1 (d, 1H, Ar-H), 8.17 (d, 1H, Ar-H), 8.02 (s, 1H, pyranone-H), 8.51 (s, 1H, Pyrimidinone H); MS (m/z): 352 $[M+H]^+$.

(E)-7-(2-(6,8-dimethoxy-4-oxo-4H-chromen-2-yl)vinyl)-5H-thiazolo[3,2-a]pyrimidin-5-one (5l): Yellow solid; Yield: 75%; M.p.: 131-133°C; IR (KBr, cm^{-1}): 1678 (C=O), 3035 (Ar-H), 1636 and 1595 (C=C), 1473 (C=N), 1338 (C-S); ^{1}H-NMR (400 MHz, DMSO-d_6), δ=3.73 (s, 3H, OCH_3), 3.93 (s, 3H, OCH_3), 6.33 (s, 1H, Ar-H), 6.98 (s, 1H, Ar-H), 7.24 and 7.30 (d, 2H, olefinic H), 7.2 (s, 1H, pyranone-H), 8.17 (d, 1H, Thiazole H), 8.02 (s, 1H, Pyrimidinone H), 6.90 (d, 1H, Thiazole H); MS (m/z): 383 $[M+H]^+$.

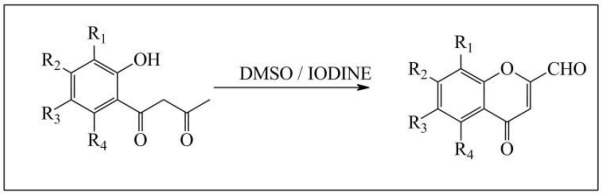
RESULTS AND DISCUSION

In brief, the synthetic program started with substituted 2-hydroxy acetophenone. Commercially available various 2-hydroxy acetophenone initially was treated with acetyl chloride in pyridine to afford acetic acid-2-acetyl phenyl ester intermediate (1) (Scheme 1).



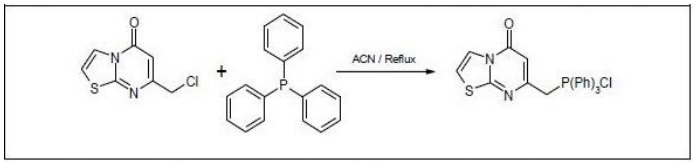
Scheme 1: Substituted acetic acid-2-acetyl phenyl ester synthesis (1)

Intermediate 1 upon treatment with KOH in ethanol water mixture gave substituted 1-(2-hydroxy-phenyl)-butane-1,3-dione (Scheme 2).



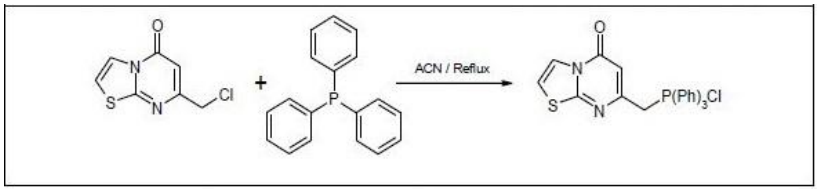
Scheme 2: Substituted 1-(2-hydroxy-phenyl)-butane-1,3dione synthesis (2)

It was then further cyclized in DMSO using catalytic iodine to substituted 4-oxo-4H-chromene-2-carbaldehyde (3) (Scheme 3 and Table 1).



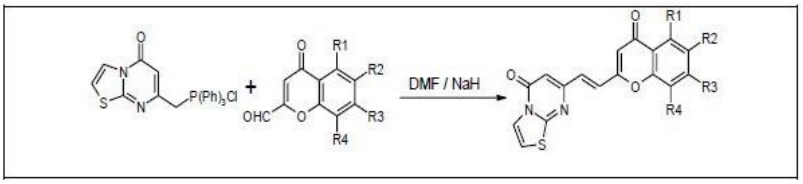
Scheme 3: Substituted 4-oxo-4H-chromene-2-carbaldehyde (3)

Commercially available 7-(chloromethyl)-5H-thiazolo (3,2-a)Pyrimidin-5-one and triphenyl phospine was heated at reflux condition and precipitation was collected after cooling and filtration to yield the corresponding 5-oxo-5H-[1, 3] thiazolo[3,2-a]pyrimidin-7-yl methyl triphenyl phosphonium chloride (4) in the expected yield (Scheme 4).



Scheme 4: 5-oxo-5H-[1, 3] thiazolo [3,2-a]pyrimidin-7-yl methyl triphenyl phosphonium chloride (4) synthesis

Finally, 5-oxo-5H-[1,3] thiazolo[3,2-a]pyrimidin-7-yl methyl triphenyl phosphonium chloride (D) and substituted 4-oxo-4H-chromene-2-carbaldehyde (C) was condensed together to afford the targeted compound 5(a-l) (Scheme 5 and Table 1).



Scheme 5: Condensation of 3 and 4 to afford substituted chromone thiazolo pyrimidinone (5a-l)

The progress of all reactions was monitored by thin layer chromatography. The synthesized derivatives 5 (a-l) were isolated in moderate to good yield.

Table 1: Substitution of 5(a-l) across R_1-R_4

S. No.	Sample	R_1	R_2	R_3	R_4
1	5a	H	Cl	H	H
2	5b	H	Cl	CH_3	H
3	5c	H	Br	H	H
4	5d	H	I	H	H
5	5e	H	H	CH_3	H
6	5f	H	Cl	CH_3	H
7	5g	H	Br	CH_3	H
8	5h	H	I	CH_3	H
9	5i	Cl	H	Cl	H
10	5j	CH_3	H	CH_3	H
11	5k	H	H	OCH_3	H
12	5l	H	OCH_3	H	OCH_3

While synthesizing the molecules 5(a-l) rationally, we tried to combine biologically active heteroatomic bicyclic pyrimidone unit with chromone moiety. The spacer unit (olefin) was introduced in between to avoid the steric obstacles (Figure 1). Variations in the molecules were obtained across the benzene ring of chromone unit. The aromatic unit along with chromone was introduced for lipophilicity.

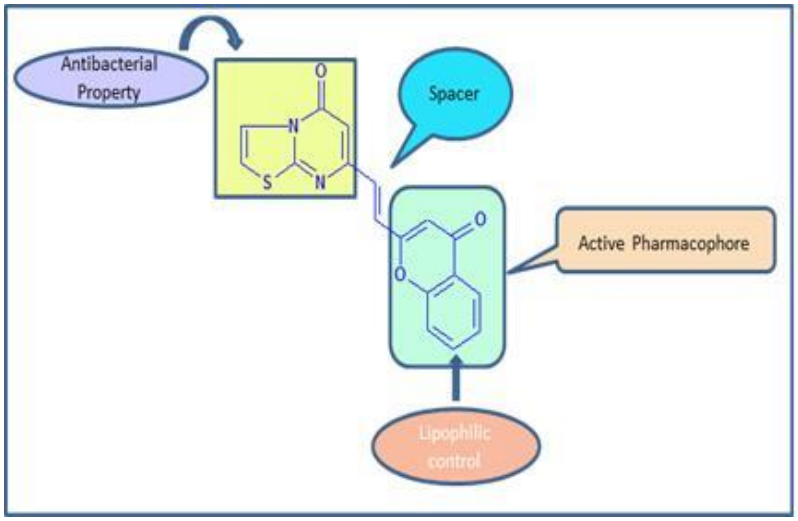


Figure 1: Essential elements of synthesized molecules

Antimicrobial activity

Applying the agar plate diffusion technique, all the synthesized compounds (5a-l) were screened in their *in vitro* antibacterial activity against Gram-positive bacteria and Gram-negative bacteria. The antibacterial activity was evaluated against different bacterial strains such as *Staphylococcus aurous* (ATCC 9027), *Bacillus subtilis* (ATCC 6633) and *Escherichia coli* (ATCC 8789), *Pseudomonas aeruginosa* (ATCC 9027) and *Salmonella abony* (NCTC-6017). Minimum Inhibitory Concentration (MIC, l g/ml) of antibacterial activity was determined using broth dilution method. Ciprofloxacin was used as a standard drug for the comparison of antibacterial activity (Table 2).

Table 2: Antimicrobial activity of synthesized compounds (5a-l)

S. No.	Compound No.	Inhibition zone diameter (mm)						
		I	II	III	IV	V	VI	VII
1	5a	10	8	9	8	8	11	9
2	5b	10	9	6	10	9	8	10
3	5c	9	11	15	9	10	12	11
4	5d	16	12	11	10	12	15	13
5	5e	12	13	11	14	13	11	11
6	5f	11	11	14	12	15	13	10
7	5g	12	15	12	14	14	13	14
8	5h	11	14	14	12	10	10	11
9	5i	12	12	12	11	12	12	10
10	5j	10	11	9	10	10	11	8
11	5k	11	11	6	8	9	8	10
12	5l	9	12	6	8	9	8	10
13	Ciprofloxacin	-	18	-	14	16	15	14

Fungus culture: I-*Aspergillus niger*, II -*Bacillus subtilis*, III-*Candida albicans*, IV-*Escherichia coli*, V-*Pseudomonas aeruginosa*, VI-*Salmonella abony*, VII-*Staphylococcus aureus*

The antifungal activity was evaluated against different fungal strains such as *C. albicans* and *A. niger*. MIC values of antifungal activity were determined using standard agar dilution method. Fluconazole is used as standard drugs for the comparison of antifungal activity. DMSO is used as solvent control. From the antimicrobial testing compounds 5(a-l), it is observed that all the newly synthesized compounds shows excellent to moderate level of antibacterial and antifungal activity shown by Table 2. The antimicrobial activity data (Table 2), reveals that compounds 5d, 5e, 5f, 5g, 5h and 5i, having thiazolo [3,2-a] pyrimidinone moiety, were found to be most active and potent as antimicrobial agents, among them 5g have been identified as the most prominent results among the series indicating the future scope for optimization. The structure activity relationship of the series can be explained as:

Effect of alkyl substituent: The chromone thiazolo pyrimidinone gave more potent molecules for the antibacterial activity. The replacement of hydrogen by methyl from chromone phenyl ring (5e-5h) displayed promising antibacterial and antifungal activity compared to standard drugs. However disubstituted derivative 5j was found to be less potent, may be due to introduction of dimethyl groups on ring.

Effect of halogen: Followed to alkyl group, the introduction of halogens across the phenyl ring showed significant impact with retain in antibacterial and antifungal activity. In this series 5g was found to be a best derivative.

Effect of methoxy: The introduction of methoxy or dimethoxy on ring (5k, 5l) reduces the overall antimicrobial activity of molecule on the tested strains as compared to other derivatives.

CONCLUSION

The synthesis of hybrid molecules of fused thiazolo [3,2-a]pyrimidone-5-one and chromone was attempted, and their subsequent evaluation as antibacterial and antifungal agent have been explained. In all the mono alkyl and halogen substitution on phenyl ring displayed decent antibacterial and antifungal profile when compare with standard reference. Moreover the disubstitution across the phenyl ring reduces the biological profile.

ACKNOWLEDGMENT

Authors are greatly thankful to the management of Maulana Azad College, Aurangabad and Principal, Bhagwan Mahavidyalaya, Ashti. Dist. Beed for the supports in the technical front.

REFERENCES

[1] D.J. Sheehan, C.A. Hitchcock, C.M. Sibley, *Clin. Microbiol. Rev*., **1999**, 12(1), 40.
[2] M.A. faller, S.A. Messer, R.J. Hollis, R.J. Jones, *Chemo. Ther*., **2001**, 45, 2862.
[3] L. Jeu, F.J. Piacenti, A.G. Lyakhovetskiy, H.B. Fung, *Clin. Ther*., **2003**, 25, 1321.
[4] G.I. Lepesheva, N.G. Zaitseva, W.D. Nes, W. Zhou, M. Arase, J. Liu, G.C. Hill, M.R. Waterman, *J. Biol. Chem*., **2014**, 281, 3577.
[5] K.A. El-Bayouki, W.M. Basyouni, *J. Sulfur Chem*., **2010**, 31, 551
[6] H. Nagarajaiah, I. Khazi, N.S. Beghum, *J. Chem. Sci*., **2012**, 124, 847.
[7] B. Tozkoparan, M. Ertan, B. Krebs, M. Läge, P. Kelicen, R. Demirdamar, *Arch. Pharm.*, **1998**, 331, 201.
[8] B. Tozkoparan, M. Ertan, P. Kelicen, R. Demirdamar, *Farmaco*., **1999**, 54, 588.
[9] E. Jeanneau-Nicolle, M. Benoit-Guyod, A. Namil, G. Leclerc, *Eur. J. Med. Chem.*, **1992**, 27, 115.
[10] B. Pan, R. Huang, L. Zheng, C. Chen, S. Han, D. Qu, M. Zhu, P. Wei, *Eur. J. Med. Chem*., **2011**, 46, 819.
[11] M. Ghorab, S. Abdel-Gawad, M. El-Gaby, *Farmaco.*, **2010**, 55, 249.
[12] S. F. Mohamed, E.M. Flefel, A.E.G. E. Amr, D.N.A. El-Shafy, *Eur. J. Med. Chem*., **2010**, 45, 1494.
[13] S. Maddila, G. Damu, E. Oseghe, O. Abafe, C.V. Rao, P. Lavanya, *J. Korean. Chem. Soc*., **2012**, 56, 334.
[14] E. Flefel, M. Salama, M. El-Shahat, M. El-Hashash, A. El-Farargy, *Phosphorus. Sulfur. Silicon. Relat. Elem*., **2007**, 182, 1739.
[15] F.A. Al-Omary, G.S. Hassan, S.M. El-Messery, H.I. El-Subbagh, *Eur. J. Med. Chem*., **2012**, 47, 65.
[16] K. Danel, E.B. Pedersen, C. Nielsen, *J. Med. Chem*., **1998**, 41, 191.

[17] A. Balkan, S. Uma, M. Ertan, W. Wiegrebe, *Pharmazie*., **1992**, 47, 687.
[18] J.C. Geist, S. Lauw, V. Illarionova, B. Illarionov, M. Fischer, T. Gräwert, F. Rohdich, W. Eisenreich, J. Kaiser, M. Groll, *Chem. Med. Chem*., **2010**, 5, 1092.