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RESEARCH ARTICLE

Design, synthesis, spectral analysis and *in vitro* microbiological evaluation of 2-phenyl-3-(4,6-diarylpyrimidin-2-yl)thiazolidin-4-ones

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Abstract

A series of novel 2-phenyl-3-(4,6-diarylpyrimidin-2-yl)thiazolidin-4-ones **23–33** were synthesized, and studied for their *in vitro* antibacterial and antifungal activities against clinically isolated strains. Generally compounds possessing electron donating groups showed good antibacterial activity. Compound **31**, which contains both electron withdrawing chloro and electron donating methyl groups showed potent activity against all the tested Gram positive and Gram negative bacterial strains whereas compounds **32** and **33** which contain electron donating methoxy functional group at the *para* position of the phenyl ring attached to pyrimidine ring showed promising activity against *S. aureus*, *S. typhi* and *E. coli*. Compounds **32** and **33**, both containing electron withdrawing groups (-Cl, -F) showed excellent activities against all the tested *A. flavus*, *Mucor*, *Rhizopus* and *M. gypseum* fungal strains. While against *Mucor*, compound **27** which contains an electron donating methyl group at the *para* position of the phenyl ring attached to pyrimidine ring showed promising activity. Also compound **31**, which contains both electron withdrawing chloro and electron donating methyl groups showed potent activity against *A. flavus* and *Rhizopus*.

Keywords: 2-phenyl-3-(4,6-diarylpyrimidin-2-yl)thiazolidin-4-ones; 2-amino-4,6-diaryl-pyrimidines; thioglycolic acid; antibacterial activity; antifungal activity

Introduction

Various 4-thiazolidinones have attracted considerable attention as they are endowed with wide range of pharmacological activities. Peptidoglycan is an essential component of the cell wall of both Gram-positive and Gram-negative bacteria. 4-Thiazolidinones have been reported as novel inhibitors of the bacterial enzyme Mur B which is a precursor, acting during the biosynthesis of peptidoglycan [1]. A wide variety of biological properties such as hypolipidaemic [2], antidegenerative [3], muscarinic receptor 1 agonist [4], antiproteolytic [5], anti-inflammatory [6], antiviral [7], antifungal [8], antibacterial [9], antitubercular [10], anticonvulsant [11], respiratory [12] and hypnotic [13] activities have been reported for 4-thiazolidinones.

Pyrimidines are the basic nucleus in nucleic acids and have been associated with a number of biological

activities. Substituted aminopyrimidine nuclei are common in marketed drugs such as anti-atherosclerotic aronixil, anti-histaminic thonzylamine, anti-anxiolytic buspirone, anti-psoriatic enazadrem, and other medicinally relevant compounds. Some notable biological activity of pyrimidine derivatives include adenosine receptor antagonists [14], kinase inhibitors [15], analgesic [16], anti-inflammatory [16], inhibitors of cyclin-Dependent kinases 1 and 2 [17], calcium channel antagonist [18], antihistaminic [19], antitubercular [20] activities.

Recently, we exploited the synthesis of 6-aryl-1,2,4,5-tetrazinane-3-thiones [21], fused indazoles [22], 2,6-diaryl-piperidin-4-one derivatives [23–25] with a view to incorporate various other bioactive heterocyclic nucleus such as 1,2,3-selenadiazoles, 1,2,3-thiadiazoles, diazepans intact for evaluation of associated antibacterial and antifungal activities.

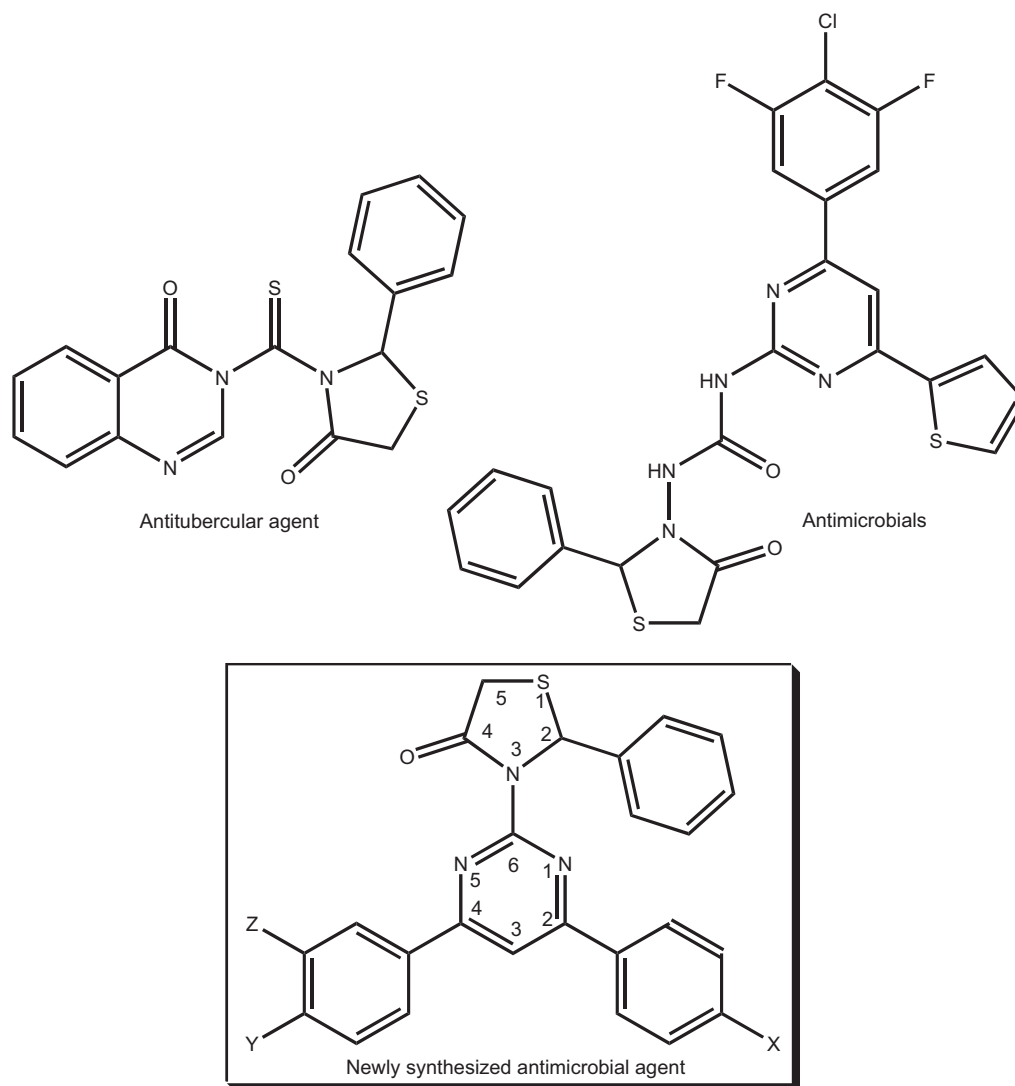


Figure 1. Synthetic compounds having the core structure with antituberculosis and antimicrobial activity.

Among the various substituted thiazolidin-4-one compounds, pyrimidine moiety present thiazolidine-4-one compound exhibit strong tuberculosis [26] and antimicrobial activity [27]. In the interest of above, we planned to synthesize a system, which comprises both 4-thiazolidinones and 2-amino-4,6-diarylpyrimidine components together to give a compact structure like title 2-phenyl-3-(4,6-diarylpyrimidin-2-yl)thiazolidin-4-ones (Figure 1).

Experimental

Chemistry

TLC was performed to assess the reactions and the purity of the products. All the reported melting points were taken in open capillaries and were uncorrected. IR spectra were recorded in KBr (pellet forms) on a Nicolet-Avatar-330 FT-IR spectrophotometer and noteworthy absorption values (cm^{-1}) alone are listed. ^1H and ^{13}C NMR spectra were recorded at 400 MHz and 100 MHz respectively on Bruker AMX 400 NMR spectrometer using $\text{DMSO}-d_6$ as solvent. The ESI +ve

MS spectra were recorded on a Bruker Daltonics LC-MS spectrometer. Satisfactory microanalysis was obtained on Carlo Erba 1106 CHN analyzer.

Adopting the literature reports 1,3-diaryl-prop-2-en-1-ones **1-11** [28] and 2-amino-4,6-diarylpyrimidines **12-22** [29], were synthesized.

General method for the synthesis of 2-phenyl-3-(4,6-diphenylpyrimidin-2-yl)thiazolidin-4-one **23**

To an ice cold stirred solution of 2-amino-4,6-diphenylpyrimidine in dry dichloromethane was added benzaldehyde in drops followed by dicyclohexylcarbodiimide (DCC). After five min. thioglycolic acid was added and stirring was continued for additional 5 h at 0°C . Then the reaction mixture was filtered to remove dicyclohexyl urea followed by washing with 5% citric acid, 10% sodium bicarbonate, brine solution, finally with water and dried over anhydrous sodium sulfate. After evaporation of the solvent under reduced pressure, a gummy mass was obtained, which was solidified on treatment of petroleum ether (bp $40^\circ\text{--}60^\circ$). Final purification of

2-phenyl-3-(4,6-diphenylpyrimidin-2-yl)thiazolidin-4-one **23** was done by column chromatography using silica gel (100-200 mesh), with ethyl acetate-Petroleum ether (bp40-60) in the ratio (2:8) as eluent. IR (KBr) (cm^{-1}): 3125, 3033, 2927, 2851, 1716, 1627, 1576, 1350, 710, 698, 649; ^1H NMR (δ ppm): 3.21 (d, 1H, CH_{2a} at H_{5a} , $J = 15.37\text{Hz}$), 3.38 (d, 1H, CH_{2e} at H_{5e} , $J = 15.37\text{Hz}$), 5.25 (s, 1H, CH at H_2), 7.19-8.37 (m, 16H, H_{arom}). A singlet for CH proton at position 5' of pyrimidine moiety is merged with aromatic protons. ^{13}C NMR (δ ppm): 34.0 C-5, 62.5 C-2, 108.1 C-5', 131.4 C-2'', 125.9-128.8 $-\text{C}_{\text{arom}}$, 139.1 C-4', 139.1 C-6'', 161.3 C-4', 161.3 C-6', 163.8 C-2', 170.6 C-4.

The compounds **24-33** were similarly synthesized.

3-(4-(4''-chlorophenyl)-6'-phenylpyrimidin-2'-yl)-2-phenylthiazolidin-4-one. **24** IR (KBr) (cm^{-1}): 3120, 3033, 2927, 2851, 1696, 1627, 1575, 1310, 894, 710, 650, 647; ^1H NMR (δ ppm): 3.22 (d, 1H, CH_{2a} at H_{5a} , $J = 15.37\text{Hz}$), 3.39 (d, 1H, CH_{2e} at H_{5e} , $J = 15.34\text{Hz}$), 5.27 (s, 1H, CH at H_2), 7.31-8.44 (m, 15H, H_{arom}). A singlet for CH proton at position 5' of pyrimidine moiety is merged with aromatic protons. ^{13}C NMR (δ ppm): 33.9 C-5, 62.6 C-2, 108.8 C-5', 127.5-133.1 $-\text{C}_{\text{arom}}$, 131.4 C-2'', 135.9 *ipso* C, 139.1 C-4'', 139.7 C-6'', 164.9 C-4'', 165.0 C-6', 162.9 C-2', 170.6 C-4.

3-(4'-(3''-chlorophenyl)-6'-phenylpyrimidin-2'-yl)-2-phenylthiazolidin-4-one. **25** IR (KBr) (cm^{-1}): 3115, 3033, 2927, 2850, 1714, 1627, 1575, 1344, 894, 767, 690, 648; ^1H NMR (δ ppm): 3.22 (d, 1H, CH_{2a} at H_{5a} , $J = 15.36\text{Hz}$), 3.39 (d, 1H, CH_{2e} at H_{5e} , $J = 15.37\text{Hz}$), 5.27 (s, 1H, CH at H_2), 7.21-8.24 (m, 15H, H_{arom}). A singlet for CH proton at position 5' of pyrimidine moiety is merged with aromatic protons. ^{13}C NMR (δ ppm): 33.9 C-5, 62.4 C-2, 108.9 C-5', 124.6-129.0 $-\text{C}_{\text{arom}}$, 130.6 *ipso* C, 131.5 C-2'', 139.0 C-4'', 141.8 C-6'', 164.9 C-4', 165.5 C-6', 162.7 C-2', 170.6 C-4.

3-(4'-(4''-methoxyphenyl)-6'-phenylpyrimidin-2'-yl)-2-phenylthiazolidin-4-one. **26** IR (KBr) (cm^{-1}): 3065, 3038, 2927, 2851, 1714, 1627, 1577, 1351, 700, 650, 649; ^1H NMR (δ ppm): 3.23 (d, 1H, CH_{2a} at H_{5a} , $J = 15.35\text{Hz}$), 3.39 (d, 1H, CH_{2e} at H_{5e} , $J = 15.27\text{Hz}$), 3.84 (s, 3H, OCH_3), 5.28 (s, 1H, CH at H_2), 7.21-8.21 (m, 15H, H_{arom}). A singlet for CH proton at position 5' of pyrimidine moiety is merged with aromatic protons. ^{13}C NMR (δ ppm): 34.5 C-5, 54.9 OCH_3 on aryl ring, 62.5 C-2, 108.7 C-5', 126.0-128.6 $-\text{C}_{\text{arom}}$, 129.1 C-2'', 139.1 C-4'', 141.5 C-6'', 164.0 C-4', 165.0 C-6', 162.3 C-2', 170.6 C-4.

3-(4'-(4''-methylphenyl)-6'-phenylpyrimidin-2'-yl)-2-phenylthiazolidin-4-one. **27** IR (KBr) (cm^{-1}): 3060, 3033, 2926, 2852, 1715, 1627, 1579, 1350, 714, 700, 643; ^1H NMR (δ ppm): 2.32 (s, 3H, CH_3), 3.23 (d, 1H, CH_{2a} at H_{5a} , $J = 15.34\text{Hz}$), 3.40 (d, 1H, CH_{2e} at H_{5e} , $J = 15.36\text{Hz}$), 5.27 (s, 1H, CH at H_2), 7.20-8.24 (m, 15H, H_{arom}). A singlet for CH proton at position 5' of pyrimidine moiety is merged with aromatic protons. ^{13}C NMR (δ ppm): 24.5 CH_3 on aryl ring, 34.1 C-5, 62.6 C-2, 108.4 C-5', 126.0-131.4 $-\text{C}_{\text{arom}}$, 133.1 C-2'', 135.9 *ipso* C, 138.7 C-4'', 139.1 C-6'', 164.9 C-4', 165.5 C-6', 162.6 C-2', 170.8 C-4.

3-(4'-(4''-fluorophenyl)-6'-phenylpyrimidin-2'-yl)-2-phenylthiazolidin-4-one. **28** IR (KBr) (cm^{-1}): 3071, 3027, 2928, 2852, 1712, 1626, 1575, 1352, 836, 769, 698; ^1H NMR (δ ppm): 3.20 (d, 1H, CH_{2a} at H_{5a} , $J = 15.24\text{Hz}$), 3.37 (d, 1H,

CH_{2e} at H_{5e} , $J = 15.28\text{Hz}$), 5.26 (s, 1H, CH at H_2), 6.64-8.19 (m, 15H, H_{arom}). A singlet for CH proton at position 5' of pyrimidine moiety is merged with aromatic protons. ^{13}C NMR (δ ppm): 34.5 C-5, 62.9 C-2, 108.9 C-5', 127.3-143.1 $-\text{C}_{\text{arom}}$, 143.6 C-2'', 145.1 C-4'', 146.1 C-6'', 166.8 C-4', 167.0 C-6', 163.9 C-2', 171.4 C-4.

3-4'-phenyl-(6'-(4''-chlorophenyl)pyrimidin-2'-yl)-2-phenylthiazolidin-4-one. **29** IR (KBr) (cm^{-1}): 3071, 3027, 2926, 2852, 1721, 1627, 1576, 1398, 782, 730, 693, 582; ^1H NMR (δ ppm): 3.21 (d, 1H, CH_{2a} at H_{5a} , $J = 15.33\text{Hz}$), 3.38 (d, 1H, CH_{2e} at H_{5e} , $J = 15.32\text{Hz}$), 5.25 (s, 1H, CH at H_2), 7.15-7.93 (m, 15H, H_{arom}). A singlet for CH proton at position 5' of pyrimidine moiety is merged with aromatic protons. ^{13}C NMR (δ ppm): 34.1 C-5, 62.9 C-2, 108.9 C-5', 126.5-128.6 $-\text{C}_{\text{arom}}$, 129.2 C-2'', 139.1 C-4'', 141.9 C-6'', 164.4 C-4', 165.3 C-6', 162.5 C-2', 170.8 C-4.

3-4'-phenyl-(6'-(4''-methoxyphenyl)pyrimidin-2'-yl)-2-phenylthiazolidin-4-one. **30** IR (KBr) (cm^{-1}): 3065, 3033, 2928, 2851, 1715, 1627, 1590, 1370, 835, 770, 699, 656; ^1H NMR (δ ppm): 3.20 (d, 1H, CH_{2a} at H_{5a} , $J = 15.08\text{Hz}$), 3.37 (d, 1H, CH_{2e} at H_{5e} , $J = 15.34\text{Hz}$), 3.86 (s, 3H, OCH_3), 5.26 (s, 1H, CH at H_2), 6.97-8.20 (m, 15H, H_{arom}). A singlet for CH proton at position 5' of pyrimidine moiety is merged with aromatic protons. ^{13}C NMR (δ ppm): 34.1 C-5, 55.2 OCH_3 on aryl ring, 62.5 C-2, 108.6 C-5', 114.1-129.1 $-\text{C}_{\text{arom}}$, 129.5 C-2'', 130.2 *ipso* C, 139.2 C-6'', 146.1 C-4'', 163.8 C-4', 164.4 C-6', 161.2 C-2', 170.7 C-4.

3-(4'-(4''-chlorophenyl)-6'-(*p*-tolylpyrimidin-2'-yl))-2-phenylthiazolidin-4-one. **31** IR (KBr) (cm^{-1}): 3060, 3027, 2927, 2851, 1721, 1626, 1576, 1398, 781, 728, 694, 650; ^1H NMR (δ ppm): 2.40 (s, 3H, CH_3), 3.20 (d, 1H, CH_{2a} at H_{5a} , $J = 15.04\text{Hz}$), 3.37 (d, 1H, CH_{2e} at H_{5e} , $J = 15.11\text{Hz}$), 5.26 (s, 1H, CH at H_2), 7.18-8.33 (m, 14H, H_{arom}). A singlet for CH proton at position 5' of pyrimidine moiety is merged with aromatic protons. ^{13}C NMR (δ ppm): 25.2 CH_3 on aryl ring, 34.5 C-5, 62.9 C-2, 108.9 C-5', 131.4 C-2'', 126.1-130.4 $-\text{C}_{\text{arom}}$, 133.1 *ipso* C, 138.7 C-6'', 139.1 C-4'', 164.8 C-4', 165.0 C-6', 161.2 C-2', 170.8 C-4.

3-(4',6'-bis(*p*-chlorophenyl)pyrimidin-2'-yl)-2-phenylthiazolidin-4-one. **32** IR (KBr) (cm^{-1}): 3060, 3027, 2927, 2852, 1727, 1627, 1575, 1400, 897, 787, 730, 693; ^1H NMR (δ ppm): 3.20 (d, 1H, CH_{2a} at H_{5a} , $J = 15.21\text{Hz}$), 3.36 (d, 1H, CH_{2e} at H_{5e} , $J = 15.23\text{Hz}$), 5.26 (s, 1H, CH at H_2), 7.28-8.20 (m, 14H, H_{arom}). A singlet for CH proton at position 5' of pyrimidine moiety is merged with aromatic protons. ^{13}C NMR (δ ppm): 34.5 C-5, 62.5 C-2, 108.7 C-5', 129.1 C-2'', 126.0-128.6 $-\text{C}_{\text{arom}}$, 139.1 C-6'', 141.8 C-4'', 164.1 C-4', 161.3 C-6', 165.3 C-2', 170.9 C-4.

3-(4'-(*p*-chlorophenyl)-6'-(*p*-fluorophenyl)pyrimidin-2'-yl)-2-phenylthiazolidin-4-one. **31** IR (KBr) (cm^{-1}): 3065, 3027, 2926, 2853, 1719, 1627, 1576, 1394, 897, 833, 776, 728, 695; ^1H NMR (δ ppm): 3.18 (d, 1H, CH_{2a} at H_{5a} , $J = 14.92\text{Hz}$), 3.35 (d, 1H, CH_{2e} at H_{5e} , $J = 14.92\text{Hz}$), 5.26 (s, 1H, CH at H_2), 7.18-8.19 (m, 14H, H_{arom}). A singlet for CH proton at position 5' of pyrimidine moiety is merged with aromatic protons. ^{13}C NMR (δ ppm): 34.1 C-5, 62.6 C-2, 110.1 C-5', 133.2 C-2'', 127.3-143.1 $-\text{C}_{\text{arom}}$, 145.1 C-6'', 146.8 C-4'', 166.8 C-4', 167.0 C-6', 163.4 C-2', 171.8 C-4.

Microbiology

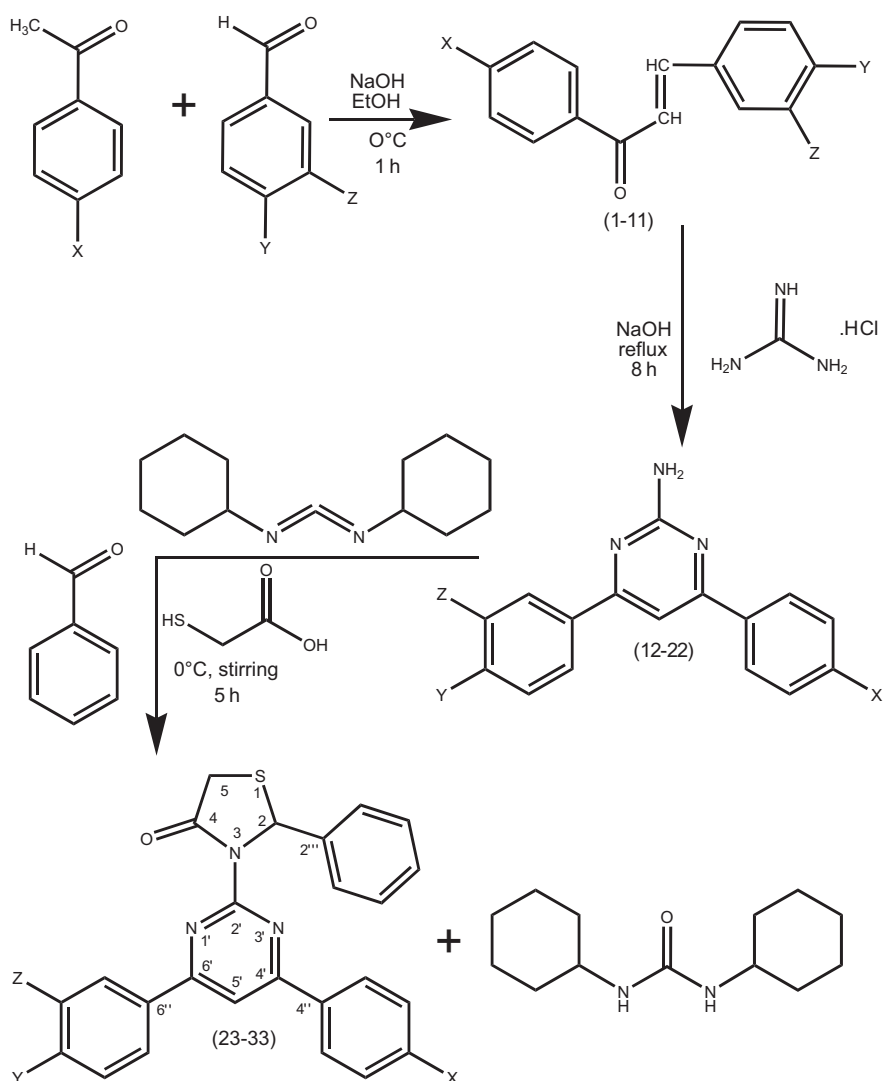
Materials

All the clinically isolated bacterial strains namely *Staphylococcus aureus*, β -*Haemolytic streptococcus*, *Vibrio cholerae*, *Salmonella typhi*, *Shigella flexneri*, *Escherichia coli*, *Klebsiella pneumonia*, *Pseudomonas aeruginosa* and fungal strains namely *Aspergillus flavus*, *Mucor*, *Rhizopus* and *Microsporium gypseum* were obtained from Faculty of Medicine, Annamalai University, Annamalainagar-608 002, Tamil Nadu, India.

In vitro antibacterial and antifungal activity

Minimum inhibitory concentration (MIC) in $\mu\text{g/mL}$ values is carried out by two-fold serial dilution method [30]. The respective test compounds **23-33** were dissolved in dimethyl sulphoxide (DMSO) to obtain 1 mg mL^{-1} stock solution. Seeded broth (broth containing microbial spores) was prepared in NB from 24 h old bacterial cultures on nutrient agar (Hi-media, Mumbai) at $37 \pm 1^\circ\text{C}$ while fungal spores from 1 to 7 days old Sabourauds agar

(Hi-media, Mumbai) slant cultures were suspended in SDB. The colony forming units (cfu) of the seeded broth were determined by plating technique and adjusted in the range of 10^4 - 10^5 cfu/mL. The final inoculum size was 10^5 cfu/mL for antibacterial assay and 1.1 - 1.5×10^2 cfu/mL for antifungal assay. Testing was performed at $\text{pH } 7.4 \pm 0.2$ for bacteria (NB) and at a $\text{pH } 5.6$ for fungi (SDB). Exactly 0.4 mL of the solution of test compound was added to 1.6 mL of seeded broth to form the first dilution. One milliliter of this was diluted with a further 1 mL of seeded broth to give the second dilution and so on till six such dilutions were obtained. A set of assay tubes containing only seeded broth was kept as control. The tubes were incubated in BOD incubators at $37 \pm 1^\circ\text{C}$ for bacteria and $28 \pm 1^\circ\text{C}$ for fungi. The minimum inhibitory concentrations (MICs) were recorded by visual observations after 24 h (for bacteria) and 72-96 h (for fungi) of incubation. Ciprofloxacin was used as standard for bacteria studies and Fluconazole was used as standards for fungal studies.



Scheme 1. Synthesis of nove 2-phenyl-3-(4,6-diarylpyrimidin-2-yl)thiazolidin-4-ones.

Results and discussion

Chemistry

Initially, attempted conversion of 2-amino-4,6-diarylpyrimidines **12-22** to 2-phenyl-3-(4,6-diarylpyrimidin-2-yl) thiazolidin-4-ones **23-33** was carried out in the absence of dicyclohexylcarbodiimide (DCC) but yields were achieved. Instead if DCC was used as a dehydrating agent, the yield of the product has been improved significantly (i.e., c. 65%) by stirring at about 0°C. The Claisen-Schmidt condensation of equimolar quantities of various *p*-substituted acetophenone with different *m*- and *p*-substituted benzaldehydes in the presence of sodium hydroxide base as a catalyst yields 1,3-diaryl-prop-2-en-1-ones **1-11**. When 1,3-diaryl-prop-2-en-1-ones **1-11** are treated with guanidine nitrate in the

presence of potassium hydroxide alkali in refluxing ethanol for 8 h gives 2-amino-4,6-diarylpyrimidines **12-22**. Novel title compounds, 2-phenyl-3-(4,6-diarylpyrimidin-2-yl) thiazolidin-4-ones **23-33** are synthesized by the addition of benzaldehyde, followed by thioglycolic acid to 2-amino-4,6-diphenylpyrimidine in dry dichloromethane at 0°C catalyzed by dicyclohexylcarbodiimide (DCC). The schematic representation and the analytical data for compounds **23-33** are given in Scheme-1 and Table-1, respectively. The importance of the title compounds is due to their diverse potential, broad-spectrum biological activity. The structure of the newly synthesized compounds **23-33** was confirmed by melting point, elemental analysis, MS, FT-IR, one-dimensional NMR (¹H & ¹³C) spectroscopic data.

Table 1. Physical and analytical data of 2-phenyl-3-(4,6-diarylpyrimidin-2-yl) thiazolidin-4-ones **23-33**.

Entry	X	Y	Z	Yield (%)	m.p° C	Elemental analysis (%)			m/z (M+1) ⁺ Molecular formula
						C Found (calculated)	H Found (calculated)	N Found (calculated)	
23	H	H	H	65	145	73.31 (73.35)	4.60 (4.64)	10.23 (10.26)	410 C ₂₅ H ₁₉ N ₃ OS
24	H	H	Cl	52	162	67.65 (67.66)	4.04 (4.06)	9.41 (9.46)	444 C ₂₅ H ₁₈ ClN ₃ OS
25	H	Cl	H	49	130	67.62 (67.66)	4.01 (4.06)	9.44 (9.46)	444 C ₂₅ H ₁₈ ClN ₃ OS
26	H	H	OCH ₃	60	110	71.03 (71.08)	4.72 (4.78)	9.51 (9.56)	440 C ₂₆ H ₂₁ N ₃ O ₂ S
27	H	H	CH ₃	65	162	73.72 (73.76)	4.92 (4.96)	9.89 (9.92)	424 C ₂₆ H ₂₁ N ₃ OS
28	H	H	F	70	104	70.23 (70.27)	4.18 (4.21)	9.79 (9.83)	428 C ₂₅ H ₁₈ FN ₃ OS
29	Cl	H	H	65	114	67.64 (67.66)	4.01 (4.05)	9.41 (9.46)	444 C ₂₅ H ₁₈ ClN ₃ OS
30	OCH ₃	H	H	58	137	71.02 (71.08)	4.72 (4.78)	9.55 (9.56)	440 C ₂₆ H ₂₁ N ₃ O ₂ S
31	Cl	H	CH ₃	55	125	68.17 (68.21)	4.32 (4.36)	9.15 (9.17)	458 C ₂₆ H ₂₀ ClN ₃ OS
32	Cl	H	Cl	60	130	62.71 (62.78)	3.52 (3.55)	8.76 (8.78)	479 C ₂₅ H ₁₇ Cl ₂ N ₃ OS
33	Cl	H	F	65	103	64.98 (65.02)	3.65 (3.68)	9.04 (9.09)	462 C ₂₅ H ₁₇ ClFN ₃ OS

Table 2. *In vitro* antibacterial activity (MIC) values for compounds **23-33**.

Compounds	Minimum Inhibitory Concentration (MIC) in µg/mL							
	<i>S.aureus</i>	<i>β-H streptococcus</i>	<i>V.cholerae</i>	<i>S.typhii</i>	<i>S.felxneri</i>	<i>E.coli</i>	<i>K.pneumonia</i>	<i>Paeruginosa</i>
23	200	100	100	50	100	50	100	200
24	100	200	50	50	100	100	200	100
25	50	- ^a	50	100	- ^a	- ^a	100	50
26	50	6.25	25	6.25	25	6.25	12.5	25
27	25	12.5	12.5	12.5	6.25	12.5	6.25	12.5
28	50	- ^a	25	50	- ^a	- ^a	50	100
29	200	100	100	100	200	200	50	50
30	25	25	50	50	100	12.5	25	12.5
31	12.5	25	12.5	6.25	6.25	25	25	6.25
32	6.25	50	50	12.5	100	12.5	200	50
33	12.5	100	50	12.5	100	12.5	100	100
Ciprofloxacin	25	50	25	50	50	25	50	12.5

^a No inhibition even at higher concentration i.e., at 200 µg/mL

Antibacterial activity

Novel 2-phenyl-3-(4,6-diarylpyrimidin-2-yl)thiazolidin-4-ones **23-33** were tested for their antibacterial activity *in vitro* against *S.aureus*, β -*H.streptococcus*, *V.cholerae*, *S.typhii*, *S.felxneri*, *E.coli*, *K.pneumonia* and *P.aeruginosa*. Ciprofloxacin was used as standard drug. Minimum inhibitory concentration (MIC) in $\mu\text{g/mL}$ values is reproduced in Table 2. Compound **23** which has no substitution at the *para* position of phenyl rings only exerted moderate activities against all the used bacterial strains. Compounds **25** and **28** which contain electron withdrawing chloro and fluoro functional group respectively at the *para* position of phenyl ring attached to pyrimidine ring did not promote much activity against β -*H.streptococcus*, *S.felxneri* and *E.coli*. Structure-activity relationship results for the synthesized compounds have shown that 2-amino-4,6-diarylpyrimidino thiazolidinones with electron donating methoxy and methyl functional group at the *para* position of the phenyl ring attached to the pyrimidine ring **26**, **27** and **30** exerted strong antibacterial activity against all the tested bacterial strains. Also compound **31**, which contain both electron withdrawing chloro and electron donating methyl groups shows potent activity against all the tested bacterial strains whereas compounds **32** and **33** which contain electron donating methoxy functional group at the *para* position of phenyl ring attached to pyrimidine ring shows promising activity against *S.aureus*, *S.typhii* and *E.coli*.

Antifungal activity

The *in vitro* antifungal activity of 2-phenyl-3-(4,6-diarylpyrimidin-2-yl)thiazolidin-4-ones **23-33** was studied against the fungal strains viz., *A.flavus*, *Mucor*, *Rhizopus* and *M.gypsuem*. Fluconazole was used as a standard drug. Minimum inhibitory concentration (MIC) in $\mu\text{g/mL}$ values is reproduced in Table 3. Compound **23** did not exhibited antifungal activity against *A.flavus* and *M.gypsuem*. Further introduction of electron withdrawing chloro functional group at the *para* position of phenyl ring attached to pyrimidine ring in compounds **24** and **29** also did not promote much activity against *A.flavus* and *M.gypsuem* while against *Mucor* and *Rhizopus*, it has registered maximum activity at 25 $\mu\text{g/mL}$. Instead if the chloro group is attached at the meta position of phenyl ring attached to pyrimidine ring in **25** promotes pronounced activity against *Mucor* at 12.5 $\mu\text{g/mL}$. Compounds **32** and **33** shows excellent activities against all the tested clinically isolated fungal strains, while against *Mucor*, compound **27** which contain electron donating methyl group at the *para* position of phenyl ring attached to pyrimidine ring showed promisable activities. The antifungal activities of these two compounds are due to the presence of two electron withdrawing chloro and fluoro functional groups attached to *para* position of the two phenyl rings. Compounds **26** and **30** which contain electron donating methoxy functional group at the *para* position of phenyl ring attached to pyrimidine ring did not promote much activity against *Mucor* and *Rhizopus*. Also

Table 3. *In vitro* antifungal activity (MIC) values for compounds **23-33**.

Compounds	Minimum Inhibitory Concentration (MIC) in $\mu\text{g/mL}$			
	<i>A.flavus</i>	<i>Mucor</i>	<i>Rhizopus</i>	<i>M. gypsuem</i>
23	– ^a	100	200	– ^a
24	200	25	25	200
25	100	12.5	50	200
26	50	200	– ^a	100
27	100	12.5	200	200
28	50	50	100	50
29	200	25	25	200
30	100	– ^a	– ^a	50
31	12.5	50	6.25	100
32	6.25	12.5	25	12.5
33	12.5	6.25	12.5	25
Fluconazole	25	25	50	50

^a No inhibition even at higher concentration i.e., at 200 $\mu\text{g/mL}$

compound **31**, which contain both electron withdrawing chloro and electron donating methyl groups shows potent activity against *A. flavus* and *Rhizopus*.

Conclusion

The microbiological screening studies carried out to evaluate the antibacterial and antifungal potencies of the newly synthesized 2-phenyl-3-(4,6-diarylpyrimidin-2-yl)thiazolidin-4-ones **23-33** are clearly known from Table 2 and Table 3. A close inspection of the *in vitro* antibacterial and antifungal activity profile in differently electron donating (CH_3 and OCH_3) and electron withdrawing ($-\text{Cl}$ and $-\text{F}$) functional group substituted phenyl rings of novel 2-aminopyrimidino thiazolidinones **23-33** exerted strong anti-bacterial activity against all the tested bacterial strains. Compound **31**, which contain both electron withdrawing chloro and electron donating methyl groups shows potent activity against all the tested bacterial strains whereas compounds **32** and **33** which contain electron donating methoxy functional group at the *para* position of phenyl ring attached to pyrimidine ring shows promising activity against *S.aureus*, *S.typhii* and *E.coli*. Results of the anti-fungal activity study show that the nature of substituents on the phenyl ring viz., methyl, fluoro and chloro functions at the *para* positions of the aryl moieties are determinant for the nature and extent of the anti-fungal activity of all the synthesized compounds **23-33** over fungal strains namely *A.flavus*, *Mucor*, *Rhizopus* and *M.gypsuem*. Compounds **26** and **30** which contain electron donating methoxy functional group at the *para* position of phenyl ring attached to pyrimidine ring did not promote much activity against *Mucor* and *Rhizopus*. Also compound **31**, which contain both electron withdrawing chloro and electron donating methyl groups shows potent activity against *A. flavus* and *Rhizopus*. The mode of action of these compounds is unknown. Further development of this group of 2-amino-4,6-diarylpyrimidino thiazolidinones may lead to compounds with better pharmacological profile than standard antibacterial and antifungal drugs.

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