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Synthesis, characterization and biological evaluation of some thiazolidinone derivatives as antimicrobial agents

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ABSTRACT

*A series of novel thiazolidinones have been synthesized by reaction of various Schiff bases of coumarin with thiolactic acid. The reaction of 4-hydroxy coumarin with $POCl_3$ yielded 4-chloro coumarin **2** and 4-chloro-3, 4', 3', 4''-tercoumarin **2a**. Compound **2** was reacted with p-phenylene diamine to yield 4-[(4-aminophenyl)amino]-2H-chromen-2-one.Various Schiff bases of coumarin were synthesized by condensation of 4-[(4-aminophenyl)amino]-2H- chromen-2-one with different aldehydes. The structures of the newly synthesized compound were confirmed by IR, ^1H NMR, ^{13}C NMR and C, H, N analysis. The thiazolidinone derivatives were evaluated for their anti bacterial and antifungal activity by broth dilution method.*

Keywords: Coumarin, Schiff bases, thiazolidinone, antibacterial, antifungal.

INTRODUCTION

4- Thiazolidinones and their derivatives are an import class of compounds in organic and medicinal chemistry. The 4-thiazolidinone ring system is a core structure in various synthetic pharmaceutical agents, displaying a broad spectrum of biological activities such as, anti-tubercular [1], anti bacterial [2], anti-HIV [3], anti-inflammatory [4], anti-mycobacterial [5], anti convulsant [6], anti histaminic [7], anti cancer [8], anti protocol [9] and analgesic [10]. 4-Thiazolidinones are derivatives of thiazolidine with carbonyl group at the 4^{th} position and formed by the attack of sulphur nucleophile on imine carbon followed by intramolecular cyclization with elimination of water.

Coumarin and its derivatives represent one of the most active classes of compound possessing a wide spectrum of biological activity [11-13]. Novobiocin and chlorobiocin are established antimicrobials containing a coumarin skeleton [14]. Many of these compounds have proved to be

active as, antibacterial [15-17], antifungal [18], anti inflammatory [19], anticoagulant [20], anti-HIV [21] and antitumor [22]; In addition, these compounds are used as additives to food and cosmetics [23].Coumarin derivatives are commonly used as optical whiteners, luminescence dyes [24], active media for lasers [25] and solar collector [26]. Various analogues of 4-substituted coumarin such as 4-chlorocoumarins exhibit antimicrobial activity. From the above line of reasoning we directed our work towards synthesis of various coumarin derivatives of biological interest using 4-chloro coumarin as a key starting material.

The aim of the present work was to synthesized new thiazolidinone derivatives containing coumarin moiety in order to find new biologically active compound. Thus, synthesis of novel 4- Thiazolidinones derivatives has been achieved.

EXPERIMENTAL SECTION

Materials and methods: All the chemicals used in the synthesis were of analytical grade. The melting points were determined in open capillary on Veego (Model: VMP-D) electronic apparatus and are uncorrected. The IR spectra of synthesized compounds were recorded on Shimadzu 8400-S FT-IR spectrophotometer using potassium bromide. To monitor the reactions, as well as, to establish the identity and purity of reactants and products, thin layer chromatography was performed on microscopic glass slides (2x7.5 cm) coated with silica gel-G, using toluene-acetone, benzene-ether and chloroform-methanol, as the solvent systems and spots were visualized under UV radiation. Nuclear magnetic resonance spectra were recorded on Varian 400 MHz model spectrometer using DMSO as a solvent and TMS as internal reference (Chemical shifts in δ ppm). All new compounds were analyzed for C, H, and N and the results are in acceptable range.

2.1-Material:

4-Hydroxy coumarin, triethyl amine (TEA), $POCl_3$, *p*-phenylene diamine, aldehydes, thiolactic acid.

2.2-Synthesis of 4-chloro coumarin (2)

4-Hydroxycoumarin **1** (30 g, 0.185 mol) and 70 mL $POCl_3$ were refluxed for 1h, cooled, and slowly poured into crushed ice (700 g) with vigorous stirring. The solid was collected by filtration and washed successively with ice-water. Azeotropic distillation with n-hexane, hot filtration of the by-product (15 g, 17 %), followed by evaporation of solvent and crystallization yielded (21.9 g, 65 %) of 4-chloro coumarin with m.p. 87-89 °C [27]; IR (KBr, cm^{-1}) 1664.62(C=O of coumarin), 773.48 (Ar-C-Cl);^{1}H-NMR (400 MHz, DMSO-d_6) δ 7.30-7.91 (m, 3H, Ar-H), 7.93 (d, 1H, H at C-5 of coumarin), 5.75 (s, 1H, H at C-3 of coumarin); ^{13}C NMR 117.22, 118.14, 124.87, 125.84, 130.18, 146.04, 149.04, 149.22, 161.23. Anal. Calcd. For $C_9H_5ClO_2$: C, 59.86; H, 2.79. Found C, 59. 88; H, 2. 76.

4-chloro-3, 4', 3', 4''-tercoumarin (by-product) **(2a):** crystallization from acetic acid gave yellowish crystals, m.p. 322-327 °C. IR (KBr, cm^{-1}) 769.62(C-Cl), 1718 (C=O), 1593-1625 (Aromatic -CH str.), 3039-3080 (C=C), 1187 (C-O str.); ^{1}H-NMR (400 MHz, DMSO- d_6) δ 7.46-7.92 (m, 9H, Ar-H), 7.27 (s, 1H, 3'-H); ^{13}C NMR 114.56, 117.60, 118.01, 118.30, 118.83, 118.96, 120.05, 123.40, 124.83, 125.55, 126.00, 126.10, 126.52, 126.69, 132.59, 133.32, 136.13, 149.96, 151.12, 151.95, 156.75, 157.00, 161.80, 163.25. Anal. Calcd. For $C_{27}H_{13}ClO_6$: C, 69.16; H, 2.79.Found C, 69.20; H, 2.75.

2.3-Synthesis of 4-[(4-Aminophenyl)amino]-2H-chromen-2-one (3):
To a boiling solution of the 4-chloro coumarin (10 g, 0.05mol) and little amount of Triethyl amine in ethanol (30 mL) was added to a boiling solution of *p*-phenylene diamine (6.09 g, 0.05mol) in ethanol (30 mL). The mixture was refluxed for 1h and left at room temperature for 4-5 h. The precipitate was separated and recrystallized from DMF. Yield:78 %; m.p. 265-273 ^{0}C; IR (KBr, cm^{-1}) 3341.78 (NH str. for 2^0), 3290.67, (NH for 1^0), 1664.62(C=O of coumarin); ^{1}H-NMR (400 MHz, DMSO- d_6) δ 6.53-7.26 (m, 7H, Ar-H), 3.31(s, 2H, NH_2), 3.76 (s,1H,C-NH), 7.93 (d, 1H, H at C-5 of coumarin), 5.75 (s, 1H, H at C-3 of coumarin); ^{13}C NMR 88.22, 116.51, 118.91, 121.80, 123.59, 124.25, 125.79, 131.84, 132.55, 145.13, 149.08, 155.32, 161.98. Anal. Calcd. For $C_{15}H_{12}N_2O_2$: C, 71.42; H, 4.79; N, 11.10. Found C, 71.40; H, 4.82; N, 11.06.

2.4-General procedure for the synthesis of Schiff bases (4a-i)
To a solution of compound **3** (1.36g; 0.01mol) in absolute ethanol (50 mL), containing a catalytic amount of piperidine, equimolecular amount of the appropriate aldehydes (for e.g. benzaldehyde) was added. The reaction mixture was heated under refluxed for 8-10 h. It was then cooled at room temperature, poured into crushed ice, filtered, washed, dried and recrystallized from DMF to yield 4-[(4-{[(*E*)-phenylmethylidene]amino}phenyl)amino]-2*H*-chromen-2-one. Other Schiff bases were obtained in similar manner.

2.5-General procedure for the synthesis of thiazolidinone (5a-i)
A mixture of compound **4a** and thiolactic acid in dry benzene (80) mL was refluxed for 12h. Water formed during the reaction was removed azeotropically by Dean-Stark apparatus. Progress of the reaction the reaction was checked by TLC using benzene-ether as eluent. After the completion of reaction benzene was removed by distillation to give solid, which was dissolved in methanol (70 mL). This solution was warmed and treated with sodium bicarbonate solution to remove unreacted acid. The solid obtained was filtered, washed with ether and purified by crystallization from methanol to give **5a**. Similarly, other compounds **(5b-5i)** have been synthesized.

2.6-Characteriaztion of synthesized compounds (5a-i)

5-Methyl-3-[4-(2-oxo-2H-chromen-4-ylamino)-phenyl]-2-phenyl-thiazolidin-4-one ***(5a)***
Yield: 72%; m.p. 250-255^{0}C ; IR (KBr,cm^{-1}) : 3292.50 (N-H str.), 1728.22 (C=O of β-lactum), 1664.62 (C=O of coumarin); ^{1}H -NMR (400 MHz, DMSO- d_6) δ 6.44-7.70 (m,13H,Ar-H); 3.76 (s,1H,C-NH); 8.27 (d, 1H, H at C-5 of coumarin), 5.77 (s, 1H, H at C-3 of coumarin), 1.75 (s,3H,CH_3); ^{13}C NMR 17.80, 45.60, 65.70, 116.50, 118.75, 122.70, 123.75, 123.80, 124.20, 125.90, 128.30, 132.60, 134.70, 139.80, 141.10, 152.75, 160.80, 174.60. Anal. Calcd. for = $C_{25}H_{20}N_2O_3S$ C, 70.07; H, 4.70; N, 6.54. Found: C, 70.08; H, 4.70; N, 6.52.

5-Methyl-2-(4-nitro-phenyl)-3-[4-(2-oxo-2H-chromen-4-ylamino)-phenyl]-thiazolidin-4-one ***(5b)***
Yield: 65%; m.p. 238-242^{0}C ; IR (KBr,cm^{-1}) : 3292.50 (N-H str.), 1730.48 (C=O of β-lactum), 1664.62 (C=O of coumarin), 1546.90 cm^{-1}(N=O str.)**;** ^{1}H -NMR (400 MHz, DMSO- d_6) δ 6.44-7.90 (m,12H,Ar-H); 3.76 (s,1H,C-NH); 8.27 (d, 1H, H at C-5 of coumarin), 5.77 (s, 1H, H at C-3 of coumarin),1.72 (s,3H,CH_3) ; ^{13}C NMR 17.86, 45.85, 65.70, 86.20, 116.46, 118.90, 122.60, 123.05, 123.60, 123.75, 124.20, 126.20, 132.60, 134.68, 139.80, 145.20, 149.06, 153.70, 160.80, 174.65. Anal. Calcd. For = $C_{25}H_{19}N_3O_5S$: C, 63.41; H, 4.04; N, 8.87. Found: C, 63.40; H, 4.04; N, 8.87.

5-Methyl-2-(3-nitro-phenyl)-3-[4-(2-oxo-2H-chromen-4-ylamino)-phenyl]-thiazolidin-4-one ***(5c)***
Yield: 70%; m.p. 240--245^{0}C ; IR (KBr,cm^{-1}) : 3292.50 (N-H str.), 1724.22 (C=O of β-lactum), 1664.62 (C=O of coumarin, 1540.12 cm^{-1}(N=O str.) ; ^{1}H -NMR (400 MHz, DMSO- d_6) δ 6.44-7.90

(m,12H,Ar-H); 3.76 (s,1H,C-NH); 8.27(d, 1H, H at C-5 of coumarin), 5.77 (s, 1H, H at C-3 of coumarin), 1.70 (s,3H,CH_3) ;^{13}C NMR 17.88, 45.84, 65.70, 86.22, 116.40, 118.80, 122.62, 123.05, 123.60, 123.73, 124.18, 126.30, 132.60, 134.72, 139.84, 145.20, 149.08, 153.65, 160.80, 174.68. Anal. Calcd. For = $C_{25}H_{19}N_3O_5S$: C, 63.41; H, 4.04; N, 8.87. Found: C, 63.42; H, 4.04; N, 8.86.

2-(3,4-Dimethoxy-phenyl)-5-methyl-3-[4-(2-oxo-2H-chromen-4-ylamino)-phenyl]-thiazolidin-4-one ***(5d)***

Yield: 62%; m.p. 259-264^{0}C ; IR (KBr,cm^{-1}) : 3290.50 (N-H str.), 1746.50 (C=O of β-lactum), 1664.62 (C=O of coumarin), 1290.40 cm^{-1}(Ar-OCH_3)**** ; ^{1}H -NMR (400 MHz, DMSO- d_6) δ 6.44-7.65 (m,11H,Ar-H); 3.76 (s,1H,C-NH); 8.27 (d, 1H, H at C-5 of coumarin), 5.77 (s, 1H, H at C-3 of coumarin), 3.40 (S,3H,-OCH_3), 1.77 (s,3H,CH_3); ^{13}C NMR 17.82, 56.80, 65.10, 86.25, 108.20, 114.95, 116.50, 117.20, 118.75, 122.45, 123.70, 123.84, 124.52, 132.59, 133.48, 149.10, 149.86, 151.39, 160.75, 174.70. Anal. Calcd. For= $C_{27}H_{24}N_2O_5S$: C, 66.38; H, 4.95; N, 5.73 Found: C, 66.40; H, 4.96; N, 5.73.

2-(4-Chloro-phenyl)-5-methyl-3-[4-(2-oxo-2H-chromen-4-ylamino)-phenyl]-thiazolidin-4-one ***(5e)***

Yield: 75%; m.p. 260-265^{0}C ; IR (KBR,cm^{-1}) : 3290.50 (N-H str.), 1730.25 (C=O of β-lactum), 1664.62 (C=O of coumarin), 768.55 cm^{-1}(Ar- C-Cl)**;** ^{1}H -NMR (400 MHz, DMSO- d_6) δ 6.40-7.68 (m,12H,Ar-H); 3.76 (s,1H,C-NH); 8.27 (d, 1H, H at C-5 of coumarin), 5.77 (s, 1H, H at C-3 of coumarin), 1.74 (s,3H,CH_3); ^{13}C NMR 17.86, 45.80, 65.59, 86.25, 116.45, 118.82, 122.34, 123.80, 124.20, 127.68, 127.90, 130.08, 132.55, 139.84, 140.25, 152.68, 160.80, 174.68. Anal. Calcd. For $C_{25}H_{19}ClN_2O_3S$: C, 64.86; H, 4.14; N, 7.66. Found: C, 64.88; H, 4.12 ; N, 7.66.

5-Methyl-3-[4-(2-oxo-2H-chromen-4-ylamino)-phenyl]-2-p-tolyl-thiazolidin-4-one ***(5f)***

Yield: 72%; m.p. 271-276^{0}C ; IR (KBR,cm^{-1}) : 3290.52 (N-H str.), 1745.62 (C=O of β-lactum), 1664.62 (C=O of coumarin), 1469.85 cm^{-1}(Ar-CH_3); ^{1}H -NMR (400 MHz, DMSO- d_6) δ 6.44-7.75 (m,12H,Ar-H); 3.76 (s,1H,C-NH); 8.27 (d, 1H, H at C-5 of coumarin), 5.77 (s, 1H, H at C-3 of coumarin), 2.16 (S,3H,Ar-CH_3), 1.75 (s,3H,CH_3); ^{13}C NMR 17.80, 21.20, 45.92, 65.20, 116.40, 118.85, 122.34, 123.85, 124.25, 126.70, 128.72, 132.55, 134.76, 135.10, 138.64, 139.85, 149.08, 152.70, 160.64, 174.64. Anal. Calcd. For = $C_{26}H_{22}N_2O_3S$: C, 70.57; H, 5.01; N, 6.33. Found: C, 70.56; H, 5.01; N, 6.33.

2-{5-Methyl-4-oxo-3-[4-(2-oxo-2H-chromen-4-ylamino)-phenyl]-thiazolidin-2-yl}-benzaldehyde ***(5g)***

Yield: 68%; m.p. 274-278^{0}C ; IR (KBr,cm^{-1}) : 3290.50 (N-H str.), 1716.47 (C=O of β-lactum), 1664.62 (C=O of coumarin), 2940.75 (Ar-CHO Str)**;** ^{1}H -NMR (400 MHz, DMSO- d_6) δ 6.40-7.80 (m,12H,Ar-H), 3.76 (s,1H,C-NH), 8.27 (d, 1H, H at C-5 of coumarin), 5.77 (s, 1H, H at C-3 of coumarin), 10.22 (s,1H,CHO), 1.75 (s,3H,CH_3); ^{13}C NMR 17.86, 45.92, 62.44, 86.14, 116.40, 118.90, 122.44, 123.75, 124.25, 124.85, 125.42, 126.98, 132.55, 133.68, 134.70, 135.75, 139.85, 141.55, 149.08, 152.72, 160.85, 174.70, 190.20. Anal. Calcd. For = $C_{26}H_{20}N_2O_4S$: C, 68.41; H, 4.42; N, 6.14. Found: C, 68.40; H, 4.42; N, 6.13.

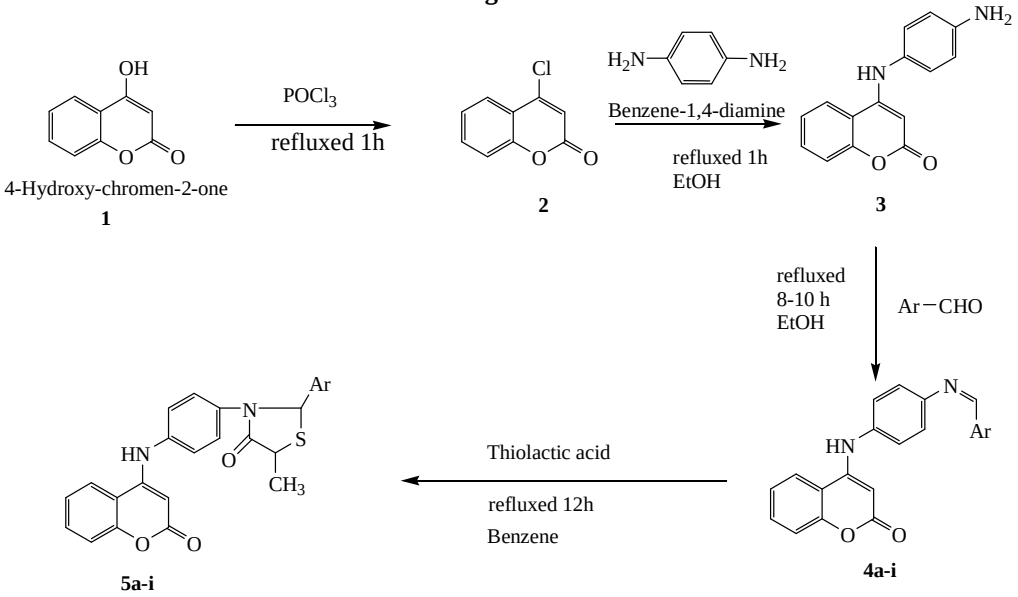
5-Methyl-2-naphthalen-1-yl-3-[4-(2-oxo-2H-chromen-4-ylamino)-phenyl]-thiazolidin-4-one ***(5h)***

Yield: 75%; m.p. 281-285^{0}C ; IR (KBr,cm^{-1}) : 3290.50 (N-H str.), 1725.33 (C=O of β-lactum), 1664.62 (C=O of coumarin), ^{1}H-NMR (400 MHz, DMSO- d_6) δ 6.40-7.90 (m,15H,Ar-H), 3.76 (s,1H,C-NH), 8.27 (d, 1H, H at C-5 of coumarin), 5.77 (s, 1H, H at C-3 of coumarin), 1.78 (s,3H,CH_3); ^{13}C NMR 17.86, 45.92, 62.12, 86.10, 118.90, 122.44, 123.75, 124.25, 126.35, 127.37, 128.89, 129.05, 129.30, 129.70, 129.90, 132.55, 134.76, 135.40, 149.10, 152.70, 160.85, 174.70. Anal. Calcd. For= $C_{29}H_{22}N_2O_3S$: C, 72.78; H, 4.63; N, 5.85. Found: C, 72.77; H, 4.63; N, 5.85.

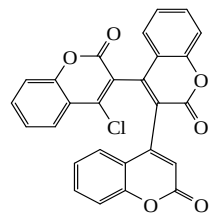
2-(2-Chloro-quinolin-3-yl)-5-methyl-3-[4-(2-oxo-2H-chromen-4-ylamino)-phenyl]-thiazolidin-4-one ***(5i)***

Yield: 70%; m.p. 291-293^{0}C ; IR (KBr,cm^{-1}) : 3290.50 (N-H str.), 1740.25 (C=O of β-lactum), 1664.62 (C=O of coumarin), 825.30 (Cl of quinoline), ^{1}H-NMR (400 MHz, DMSO- d_6) δ 6.44-8.10 (m,13H,Ar-H), 3.76 (s,1H,C-NH), 8.27 (d, 1H, H at C-5 of coumarin), 5.77 (s, 1H, H at C-3 of coumarin), 1.78 (s,3H,CH_3); ^{13}C NMR 17.86, 45.90, 86.10, 116.50, 118.23, 122.62, 123.70, 124.25, 126.30, 128.60, 128.80, 130.04, 132.55, 133.50, 135.30, 136.60, 139.55, 147.70, 150.40, 152.75, 160.85, 174.70. Anal. Calcd. For= $C_{28}H_{20}ClN_3O_3S$: C, 65.43; H, 3.92; N, 8.18. Found: C, 65.44; H, 3.92; N, 8.18.

Figure 1



Scheme: Synthesis of thiazolidinone derivatives



4-Chloro-3, 4',3',4''-tercoumarin **2a**

	Ar
a	Phenyl
b	4-Nitro phenyl
c	3-Nitro phenyl
d	3,4-dimethoxy phenyl
e	4-chloro phenyl
f	4-methyl phenyl
g	Phenyl-2-carboxaldehyde
h	Naphthyl
i	2-chloro quinonyl

2.7 Antimicrobial activity

All the synthesized compounds were tested for their antibacterial and antifungal activity (MIC-minimum inhibition concentration) in vitro by broth dilution method with two gram positive bacteria *S. aureus* and *B. subtilis* and gram negative bacteria *E. coli*, *P. aeruginosa*, and fungi species like *C. albicans, A. niger* organisms taking ciprofloxacin, ampicillin, chloramphenicol, norfloxacin, flucanazole, griseofulvin, and Nystatin. Muller Hinton broth was used as nutrient medium to grow and dilute the drug suspension for test. DMSO was used as a diluent which not effected the growth of microbes.

RESULTS AND DISCUSSION

All the reactions were carried out under conventional methods. 4-[(4-Aminophenyl)amino]-2*H*-chromen-2-one **3** was a key intermediate that required to prepare the target product. 4-Chloro coumarin **2** was prepared from 4-hydroxy coumarin **1.** But the selectivity of the reaction of **1** with $POCl_3$ was low, because a considerable amount of 4-chloro-3, 4', 3', 4''-tercoumarin was formed as a byproduct. In this method n-hexane was used to improve the yield of 4-chloro coumarin and significantly decreased yield of the by product. The key intermediate 4-[(4-aminophenyl)amino]-2*H*-chromen-2-one **3** was easily prepared from 4-chloro coumarin using little amount of triethyl amine. The IR spectra of compound **3** revealed a strong band at 3290.67 cm^{-1}confirming the presence of 2^0 –NH group and band at 3341.78 cm^{-1}indicating the presence of 1^0-NH_2 group. The IR spectrum of compound **3** showed a band in the region of 1664.62 cm^{-1}which is the characteristic for C=O of coumarin. The ^{1}H NMR data of compound **3** revealed signal between 6.53-7.26 δ ppm for aromatic protons. The IR spectra of compound **4b** revealed a characteristic band at 3296.46 cm^{-1}confirming the presence of 2^0 –NH group and there was no any band at 3341 cm^{-1}confirming that -NH_2 group of compound **3** completely reacted with –CHO group of aldehyde to form Schiff base. Stretching vibration for C=N of Schiff base present at around 1473-1602 cm^{-1}. The ^{1}H NMR data of compounds revealed signal between 6.55-7.52 δ ppm for aromatic protons. All the Schiff bases reacted with Thioglycolic acid to afford thiazolidinone derivatives. IR spectrum of the compound **5b** showed a characteristic band at 1730.48 cm^{-1} confirming the presence of C=O group thiazolidinone. The ^{1}H NMR data of compound **5b** revealed signal between 6.44-7.90 δ ppm for aromatic protons and singlet at 1.72 δ ppm for – CH_3 of thiazolidinones.

Table 1 Antimicrobial study (MIC µg/mL) of synthesized compound 4a-5i.

Minimum inhibitory concentration

Comp. no.	Ar	Gram negative		Gram positive		Fungal species	
		E. coli	*P. aeruginosa*	*S. aureus*	*B. subtilis*	*C. albicans*	*A. niger*
4a	Phenyl	500	1000	500	1000	500	1000
4b	4-Nitro phenyl	200	200	500	1000	800	1000
4c	3-Nitro phenyl	500	200	100	200	500	1000
4d	3,4-dimethoxy phenyl	200	500	1000	200	100	500
4e	4-chloro phenyl	50	100	200	100	500	>1000
4f	4-methyl phenyl	100	200	1000	500	200	500
4g	Phenyl-2-carboxaldehyde	500	1000	800	100	500	1000
4h	Naphthyl	500	250	800	100	400	1000
4i	2-chloro quinonyl	250	400	500	100	400	>1000
5a	Phenyl	400	500	400	500	800	1000
5b	4-Nitro phenyl	100	100	400	200	500	500
5c	3-Nitro phenyl	250	400	500	200	500	1000
5d	3,4-dimethoxy phenyl	250	250	500	250	500	500
5e	4-chloro phenyl	100	100	250	200	200	800
5f	4-methyl phenyl	200	100	200	400	250	500
5g	Phenyl-2-carboxaldehyde	200	250	500	250	400	1000
5h	Naphthyl	100	250	400	200	500	500
5i	2-chloro quinonyl	200	100	250	100	250	500
Ampicillin		100	100	250	100	-	-
ciprofloxacin		25	25	50	50	-	-
chloramphenicol		50	50	50	50	-	-
Norfloxacin		10	10	10	10	-	-
Griseofulvin						500	100
Nystatin						100	100
Flucanazole						10	10

All the newly synthesized compounds were screened for their antimicrobial activity. From the result in table 1 Schiff base **4e** showed excellent activity when compared with ampicillin and chloramphenicol; while **5b, 5e,** and **5h** demonstrated good activity against *E.coli* and **5b**, **5e, 5i** significant activity against *P.aeruginosa*; while **4c, 5e, 5g, 5i** showed good activity against *S.aureus* and **5i** demonstrated significant activity against *B.subtilis* when compared with standard drug ampicillin.

From the MIC results of fungal activity, Schiff base **4d** was found equipotent to Nystatin; while **4a, 4c, 4e, 4f, 4g, 4h, 4i** demonstrated significant activity. The thiazolidinones **5e, 5f,** and **5i** demonstrated good activity against *C. albicans* when compared with Griseofulvin . All remaining compounds demonstrated good to moderate activity against remaining fungal specie (*A. niger*).

CONCLUSION

A series of coumarin based thiazolidinones compounds were successfully synthesized and tested for their in vitro antimicrobial activity. Overall conclusion made for synthesized compounds are that most of the compounds were more active against *E. coli*, *S. aureus* and *B. subtilis*. Some of the compounds were found equipotent to ampicillin and found less active than other standard drugs. Most of the compounds demonstrated antifungal activity for *C. albicans* similar to that of Griseofulvin, found less active than other fungal specie (*A. niger*).

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