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SHORT COMMUNICATION

SYNTHESIS OF 2-(SUBSTITUTED PHENYL)-3-[5-(2-OXO-2*H*-CHROMEN-3-YL)-1,3,4-OXADIAZOL-2-YL]-1,3-THIAZOLIDIN-4-ONES WITH ANTIMICROBIAL ACTIVITY

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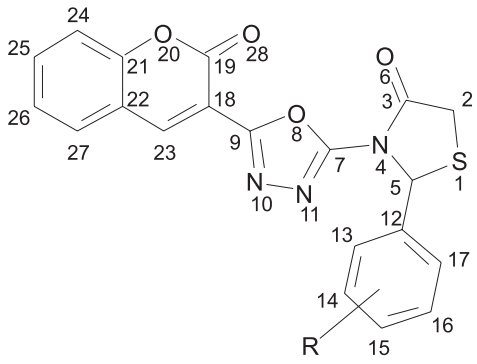
Coumarins have been reported to possess wide variety of biological activities like anti-inflammatory (1), anticonvulsant (2) and antitumor (3). The 1,3,4-oxadiazole derivatives are reported to show a broad spectrum of biological activities, which include antibacterial (4), anti-inflammatory (5), anticonvulsant (6, 7), CNS stimulant (8) and antihypertensive (9). The 1,3,4-thiazolidinone derivatives also possess activities like antibacterial (10), anticonvulsant (11), antifungal (12), antihistaminic (13) and anti HIV (14). This prompted us to synthesize and study the antimicrobial activity of compounds incorporating coumarin, 1,3,4-oxadiazole and 1,3,4-thiazolidinone moieties:



EXPERIMENTAL

All the solvents were of LR grade and were obtained from Merck, CDH and S. D. Fine Chemicals. Melting points were determined in open capillary tubes and are uncorrected. Thin layer chromatography was performed on silica gel G (Merck). The FT-IR spectra were recorded in KBr pellets on a BIO-RAD FTS 135 WIN-IR spectrophotometer. ^{1}H-NMR and ^{13}C NMR spectra were recorded on a Bruker model DPX 300 FT NMR spectrometer in (DMSO-d_6) using tetramethylsilane (Me_4Si, TMS) as an internal standard. Mass spectra were recorded at 70 eV on a Jeol JMS-D instrument fitted with a JMS 2000 data system,. All the structures of the compounds were drawn with the help of ChemDraw Ultra 9.0 (ChemOffice 2005 software).

Synthesis of ethyl-2-oxo-2*H*-chromene-3-carbxylate **1** (m.p. 120–122şC), 2-oxo-2*H*-chromene-3-carbohydrazide **2** (m.p. 136–138şC), 3-(5-amino-1,3,4-oxadiazol-2-yl)-2*H*-chromen-2-one **3** (m.p. 200–202şC) and 3-(5-{[substituted phenyl)methylene]amino}-1,3,4-oxadiazol-2-yl)-2*H*-chromen-2-ones **4** were carried out by reported methods (15–17).

General method of synthesis of 2-(substituted phenyl)-3-[5-(2-oxo-2*H*-chromen-3-yl)-1,3,4-oxadiazol-2-yl]-1, 3-thiazolidin-4-ones (5a-m) (Scheme 1)

13-(5-{[Substituted phenyl)methylene]amino}-1,3,4-oxadiazol-2-yl)-2*H*-chromen-2-one **4** (0.01 mol) and mercaptoacetic acid (0.9 g, 0.01 mol) were refluxed in the presence of catalytic amount of $ZnCl_2$ in dry 1,4-dioxane (25 mL) for 12 h. Then, the reaction mixture was cooled and poured onto crushed ice. The separated out product **5** was filtered, dried and crystallized from ethanol. The other compounds of the series were synthesized similarly.

2-(3-Nitrophenyl)-3-[5-(2-oxo-2*H*-chromen-3-yl)-1,3,4-oxadiazol-2-yl]-1,3-thiazolidin-4-one **(5a)**

Yield: 60%; m.p. 178–180ºC; R_f 0.73; IR (KBr, cm^{-1}): 3000 (C-H), 2700 (N= C-H). 1680 (C=O,

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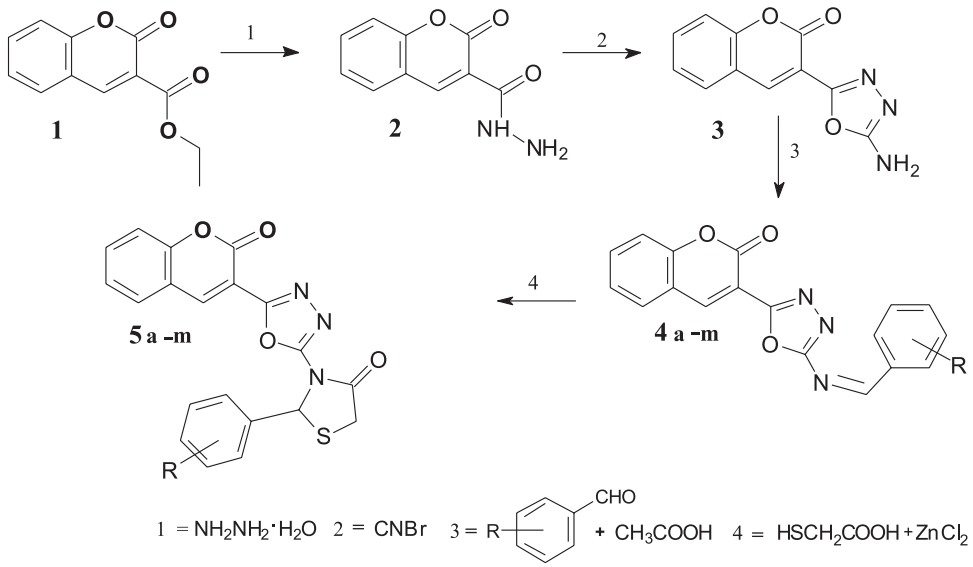

R = 5a – 3-NO_2; **5b** – 3,4$(OCH_3)_2$; **5c** – 4-OH; **5d** – 2-OH; **5e** – 2-NO_2; **5f** – 3-OH; **5g** – 4-$N(CH_3)_2$; **5h** – 4-F; **5i** – 4-OCH_3; **5j** – 2-Cl; **5k** – 3-Cl; **5l** – 4-Cl; **5m** – H

Scheme 1. Synthesis of compounds **5a-m**

coumarin), 1600 (C=C), 1350 (C-N), 1272 (C-O), 753 (=C-H). ^{1}H-NMR ($CDCl_3$, δ, ppm): 3.6 (s, 2H, β-thialactam ring); 7.0–8.3 (m, 8H, Ar-H), 8.8 (s, 1H, Ar-H, H-4), 11.3 (s, 1H, CH-Ar). ^{13}C-NMR ($CDCl_3$, δ, ppm): 33.5 (C_2), 64.3 (C_5), 121.5 (C_{24}), 122.2 (C_{22}), 122.3 (C_{15}), 125.2 (C_{13}), 125.5 (C_{26}), 126.8 (C_{27}), 128.4 (C_{25}), 129.4 (C_{18}), 129.6 (C_{16}), 134.3 (C_{17}), 140.1 (C_{12}), 146 (C_{23}), 147.8 (C_{14}), 150.1 (C_{21}), 161.9 (C_{19}), 171.2 (C_3). MS (m/z): 436 (M^+). Analysis: for $C_{20}H_{12}N_4O_6S$ calcd. C 55.04, H 2.77, N 12.84, S 7.35%; found: C 55.24, H 2.76, N 12.89, S 7.33 %.

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2-(3,4-Dimethoxyphenyl)-3-[5-(2-oxo-2*H*-chromen-3-yl)-1,3,4-oxadiazol-2-yl]-1,3-thiazolidin-4-one (**5b**)

Yield: 55%; m.p. 170–172°C; R_f 0.75; IR (KBr, cm^{-1}): 2981 (C-H), 2700 (N-C-H), 1717 (C=O, coumarin), 1456, 1489, 1508; (C=C), 1271 (C-O), 1377 (C-N), 753 (=C-H). ^{1}H-NMR ($CDCl_3$, δ, ppm): 3.3 (s, 6H, 2´OCH_3), 3.6 (s, 2H, β-thialactam ring), 6.9–7.6 (m, 7H, *J* = 10 Hz, Ar-H), 8.9 (s, 1H, Ar-H, H-4), 11.2 (s, 1H, CH-Ar). ^{13}C-NMR ($CDCl_3$, δ, ppm): 33.5 (C_2), 64.3 (C_5), 121.5 (C_{24}), 122.2 (C_{22}), 122.3 (C_{15}), 125.2 (C_{13}), 125.5 (C_{26}), 126.8 (C_{27}), 128.4 (C_{25}), 129.4 (C_{18}), 129.6 (C_{16}), 134.3 (C_{17}), 140.1 (C_{12}), 146 (C_{23}), 147.8 (C_{14}), 150.1 (C_{21}), 161.9 (C_{19}), 171.2 (C_3). MS (m/z): 451(M^+). Analysis: for $C_{22}H_{17}N_3O_6S$ calcd. C 58.53, H 3.80, N 9.31, S 7.10%; found: C 58.33, H 3.81, N 9.36, S 7.12%.

2-(4-Hydroxyphenyl)-3-[5-(2-oxo-2*H*-chromen-3-yl)-1,3,4-oxadiazol-2-yl]-1,3-thiazolidin-4-one (**5c**)

Yield: 62%; m.p. 300°C (decomp.); R_f 0.60; IR (KBr, cm^{-1}): 3600 (-OH), 3330 (C-H), 2700 (N-C-H), 1620 (C=O, coumarin), 1500, 1480 (C=C), 1350 (C-N), 1271 (C-O); 750 (=C-H). ^{1}H-NMR ($CDCl_3$, δ, ppm): 3.8 (s, 2H, β-thialactam ring), 6.9–7.4 (m, 8H, Ar-H), 7.5 (s, 1H, Ar-H, H-4), 8.7 (s, 1H, Ar-OH), 11.3 (s, 1H, CH-Ar). ^{13}C-NMR ($CDCl_3$, δ, ppm): 33.5 (C_2), 64.3 (C_5), 121.5 (C_{24}), 122.2 (C_{22}), 122.3 (C_{15}), 125.2 (C_{13}), 125.5 (C_{26}), 126.8 (C_{27}), 128.4 (C_{25}), 129.4 (C_{18}), 129.6 (C_{16}), 134.3 (C_{17}), 140.1 (C_{12}), 146 (C_{23}), 147.8 (C_{14}), 150.1 (C_{21}), 161.9 (C_{19}), 171.2 (C_3). MS (m/z): 407 (M^+). Analysis: for $C_{20}H_{13}N_3O_5S$ calcd. C 58.96, H 3.22, N 10.31, S 7.87%; found: C 58.76, H 3.20, N 10.36, S 7.85%.

2-(2-Hydroxyphenyl)-3-[5-(2-oxo-2*H*-chromen-3-yl)-1,3,4-oxadiazol-2-yl]-1,3-thiazolidin-4-one (**5d**)

Yield: 65%; m.p. 175–177°C; R_f 0.50; IR (KBr, cm^{-1}): 3600 (-OH), 3330 (C-H), 2700 (N-C-H), 1620 (C=O, coumarin), 1500, 1480 (C=C), 1350 (C-N), 1271 (C-O), 750 (=C-H). ^{1}H-NMR ($CDCl_3$, δ, ppm): 3.8 (s, 2H, β-thialactam ring), 6.9–7.4 (m, 8H, Ar-H), 7.5 (s, 1H, Ar-H, H-4), 8.7 (s, 1H, Ar-OH), 11.3 (s, 1H, CH-Ar). ^{13}C-NMR ($CDCl_3$, δ, ppm): 33.5 (C_2), 64.3 (C_5), 115.8 (C_{14}), 118 (C_{12}),

121.3 (C_{16}), 121.5 (C_{24}), 122.2 (C_{22}), 125.5 (C_{26}), 126.8 (C_{27}), 128.4 (C_{25}), 128.6 (C_{15}), 129.4 (C_{18}), 130.1 (C_{17}), 146 (C_{23}), 150.1 (C_{21}), 155.8 (C_{13}), 161.9 (C_{19}), 171.2 (C_3). MS (m/z): 407 (M^+). Analysis: for $C_{20}H_{13}N_3O_5S$ calcd. C 58.96, H 3.22, N 10.31, S 7.87%; found: C 58.76, H 3.20, N 10.36, S 7.85 %.

2-(2-Nitrophenyl)-3-[5-(2-oxo-2*H*-chromen-3-yl)-1,3,4-oxadiazol-2-yl]-1,3-thiazolidin-4-one **(5e)**

Yield: 68%; m.p. 210–212°C; R_f 0.74; IR (KBr, cm^{-1}): 3000 (C-H), 2700 (N-C-H), 1680 (C=O, coumarin), 1500 (C=C), 1377 (C-N), 1271 (C-O), 754 (=C-H). ^{1}H-NMR ($CDCl_3$, δ, ppm): 3.7 (s, 2H, CH_2- thiolactam), 7.2–7.5 (m, 8H, Ar-H), 8.7 (s, 1H, Ar-H, H-4), 11.3 (s, 1H, CH-Ar). ^{13}C-NMR ($CDCl_3$, δ, ppm): 33.5 (C_2), 64.3 (C_5), 121.5 (C_{24}), 122.2 (C_{22}), 123.8 (C_{14}), 125.5 (C_{26}), 126.8 (C_{27}), 128.1 (C_{15}), 128.4 (C_{25}), 129.4 (C_{18}), 129.5 (C_{17}), 133.4 (C_{12}), 134.8 (C_{16}), 146 (C_{23}), 149.0 (C_{13}), 150.1 (C_{21}), 161.9 (C_{19}), 171.2 (C_3). MS (m/z): 436 (M^+). Analysis: for: $C_{20}H_{12}N_4O_6S$ calcd. C 55.04, H 2.77, N 12.84, S 7.35%; found: C 55.24, H 2.76, N 12.89, S 7.32%.

2-(3-Hydroxyphenyl)-3-[5-(2-oxo-2*H*-chromen-3-yl)-1,3,4-oxadiazol-2-yl]-1,3-thiazolidin-4-one **(5f)**

Yield: 64%; m.p. 150–152°C; R_f 0.52; IR (KBr, cm^{-1}): 3000 (C-H), 2700 (N-C-H), 1621 (C=O, coumarin), 1486, 1577 (C=C), 1386 (C-N), 1271 (C-O), 750, 740 (=C-H). ^{1}H-NMR ($CDCl_3$, δ, ppm): 3.62 (s, 2H, CH_2- thiolactam), 7.0–7.4 (m, 8H, *J* = 10 Hz, Ar-H), 8.7 (s, 1H, Ar-H, H-4), 8.8 (s, 1H, Ar-OH), 11.34 (s, 1H, CH-Ar). ^{13}C-NMR ($CDCl_3$, δ, ppm): 33.5 (C_2), 64.3 (C_5), 14.3 (C_{13}), 114.3 (C_{15}), 121.3 (C_{17}), 121.5 (C_{24}), 122.2 (C_{22}), 125.5 (C_{26}), 126.8 (C_{27}), 128.4 (C_{25}), 129.4 (C_{18}), 130.1 (C_{16}), 146 (C_{23}), 150.1 (C_{21}), 158.4 (C_{14}), 161.9 (C_{19}), 171.2 (C_3). MS (m/z): 407 (M^+). Analysis: for $C_{20}H_{13}N_3O_5S$ calcd. C 58.96, H 3.22, N 10.31, S 7.87%; found: C 58.76, H 3.23, N 10.35, S 7.85 %.

2-[4-(Dimethylamino)phenyl]-3-[5-(2-oxo-2*H*-chromen-3-yl)-1,3,4-oxadiazol-2-yl]-1,3-thiazolidin-4-one **(5g)**

Yield: 60%; m.p. 180–182°C; R_f 0.57; IR (KBr, cm^{-1}): 3000 (C-H), 2720 (N-C-H), 1620 (C=O, coumarin), 1480, 1575 (C=C), 1380 (C-N), 1275 (C-O), 750 (=C-H). ^{1}H-NMR ($CDCl_3$, δ, ppm): 1.3 (s, 6H, 2´NCH_3), 3.62 (s, 2H, CH_2- thiolactam), 7.0–7.4 (m, 8H, *J* = 10 Hz, Ar-H), 8.7 (s, 1H, Ar-H, H-4), 11.3 (s, 1H, CH-Ar). ^{13}C-NMR ($CDCl_3$, δ, ppm): 33.5 (C_2), 40.2 ($C_{29, 30}$), 64.3 (C_5), 114.2 (C_{14}), 114.2 (C_{16}), 121.5 (C_{24}), 122.2 (C_{22}), 125.5 (C_{26}), 126.8 (C_{27}), 128.4 (C_{25}), 128.7 (C_{12}), 129 (C_{17}), 129.4 (C_{18}), 129.6 (C_{13}), 146 (C_{23}), 148.0 (C_{15}), 150.1 (C_{21}), 161.9 (C_{19}), 171.2 (C_3). MS (m/z): 434 (M^+). Analysis: for $C_{22}H_{18}N_4O_4S$ calcd. C 60.82, H 4.18, N 12.90, S 7.38%; found: C 60.62, H 4.17, N 12.95, S 7.40%.

2-(4-Fluorophenyl)-3-[5-(2-oxo-2*H*-chromen-3-yl)-1,3,4-oxadiazol-2-yl]-1,3-thiazolidin-4-one **(5h)**

Yield: 60%; m.p. 178–180°C; R_f 0.73; IR (KBr, cm^{-1}): 3390 (C-H), 2720 (N=C-H), 1620 (C=O, coumarin), 1500 (C=C), 1380 (C-N), 1271 (C-O), 751 (=C-H). ^{1}H-NMR ($CDCl_3$, δ, ppm): 3.2 (s, 2H, CH_2- thiolactam), 7.2–7.3 (m, 8H, Ar-H), 8.7 (s, 1H, Ar-H, H-4), 11.3 (s, 1H, CH-Ar). ^{13}C-NMR ($CDCl_3$, δ, ppm): 33.5 (C_2), 64.3 (C_5), 115 (C_{14}), 115 (C_{16}), 121.5 (C_{24}), 122.2 (C_{22}), 125.5 (C_{26}), 126.8 (C_{27}), 128.4 (C_{25}), 129.4 (C_{18}), 130.3 (C_{13}), 130.3 (C_{17}), 134.8 (C_{12}), 146 (C_{23}), 150.1 (C_{21}), 161.3 (C_{15}), 161.9 (C_{19}), 171.2 (C_3). MS (m/z): 409 (M^+). Analysis: for $C_{20}H_{12}FN_3O_4S$ calcd. C 58.68, H 2.95, N 10.26, S 7.83%; found: C 58.88, H 2.94, N 10.21, S 7.81%.

2-(4-Methoxyphenyl)-3-[5-(2-oxo-2*H*-chromen-3-yl)-1,3,4-oxadiazol-2-yl]-1,3-thiazolidin-4-one **(5i)**

Yield: 58%; m.p. 200–202°C; R_f 0.64; IR (KBr, cm^{-1}): 3000 (C-H), 2710 (N=C-H), 1680 (C=O, coumarin), 1520 (C=C), 1380 (C-N), 1220 (C-O), 754 (=C-H). ^{1}H-NMR ($CDCl_3$, δ, ppm): 3.0 (s, 3H, OCH_3), 3.2 (s, 2H, CH_2- thiolactam), 7.2–7.3 (m, 8H, Ar-H), 8.7 (s, 1H, Ar-H, H-4), 11.3 (s, 1H, CH-Ar). ^{13}C-NMR ($CDCl_3$, δ, ppm): 33.5 (C_2), 55.8 (C_{29}), 64.3 (C_5), 114 (C_{14}), 114 (C_{16}), 121.5 (C_{24}), 122.2 (C_{22}), 125.5 (C_{26}), 126.8 (C_{27}), 128.4 (C_{25}), 129 (C_{17}), 129.4 (C_{18}), 129.7 (C_{13}), 131.5 (C_{12}), 146 (C_{23}), 150.1 (C_{21}), 159 (C_{15}), 161.9 (C_{19}), 171.2 (C_3). MS (m/z): 421 (M^+). Analysis: for $C_{20}H_{12}FN_3O_4S$ calcd. C 59.85, H 3.59, N 9.97, S 7.61%; found: C 59.65, H 3.60, N 9.92, S 7.63 %..

2-(2-Chlorophenyl)-3-[5-(2-oxo-2*H*-chromen-3-yl)-1,3,4-oxadiazol-2-yl]-1,3-thiazolidin-4-one **(5j)**

Yield: 70%; m.p. 300°C (decomp.); R_f 0.80; IR (KBr, cm^{-1}): 3000 (C-H), 2700 (N=C-H), 1580 (C=O, coumarin), 1500 (C=C), 1383 (C-N), 1228 (C-O), 754, 740 (=C-H). ^{1}H-NMR ($CDCl_3$, δ, ppm): 3.2 (s, 2H, CH_2- thiolactam), 7.2–7.3 (m, 8H, Ar-H), 8.7 (s, 1H, Ar-H, H-4), 11.3 (s, 1H, CH-Ar). ^{13}C-NMR ($CDCl_3$, δ, ppm): 33.5 (C_2), 64.3 (C_5), 102.5 (C_{12}), 121.5 (C_{24}), 122.2 (C_{22}), 125.5 (C_{26}), 126.8 (C_{27}), 128.6 (C_{15}), 128.7 (C_{14}), 126.8 (C_{16}), 128.4 (C_{25}), 129.4 (C_{18}), 130.1 (C_{17}), 134 (C_{13}), 146 (C_{23}), 150.1 (C_{21}), 161.9 (C_{19}), 171.2 (C_3). MS (m/z): 425 (M^+). Analysis: for $C_{20}H_{12}ClN_3O_4S$ calcd. C 56.41, H 2.84, N 9.87, S 7.53%; found: C 56.61, H 2.83, N 9.85, S 7.55%.

2-(3-Chlorophenyl)-3-[5-(2-oxo-2*H*-chromen-3-yl)-1,3,4-oxadiazol-2-yl]-1,3-thiazolidin-4-one **(5k)**

Yield: 58%; m.p. 250–252°C; R_f 0.82; IR (KBr, cm^{-1}): 3398 (C-H), 2700 (N=C-H), 1620 (C=O, coumarin), 1500 (C=C), 1390 (C-N), str.; 1271 (C-O), 751, 740 (=C-H). ^{1}H-NMR ($CDCl_3$, δ, ppm): 3.2 (s, 2H, CH_2- thiolactam), 7.2–7.3 (m, 8H, Ar-H), 8.7 (s, 1H, Ar-H, H-4), 11.3 (s, 1H, CH-Ar). ^{13}C-NMR ($CDCl_3$, δ, ppm): 33.5 (C_2), 64.3 (C_5), 121.5 (C_{24}), 122.2 (C_{22}), 125.5 (C_{26}), 126.8 (C_{17}), 126.8 (C_{27}), 127.2 (C_{15}), 128.4 (C_{25}), 128.5 (C_{13}), 129.4 (C_{18}), 130.1 (C_{16}), 134.2 (C_{14}), 140.6 (C_{12}), 146 (C_{23}), 150.1 (C_{21}), 161.9 (C_{19}), 171.2 (C_3). MS (m/z): 425 (M^+). Analysis: for $C_{20}H_{12}ClN_3O_4S$ calcd. C 56.41, H 2.84, N 9.87, S 7.53%; found: C 56.65, H 2.82, N 9.82, S 7.54%.

2-(4-Chlorophenyl)-3-[5-(2-oxo-2*H*-chromen-3-yl)-1,3,4-oxadiazol-2-yl]-1,3-thiazolidin-4-one **(5l)**

Yield: 65%; m.p. 280–282°C; R_f 0.83; IR (KBr, cm^{-1}): 3390 (C-H), 2700 (N= C-H), 1628 (C=O, coumarin), 1500 (C=C), 1380 (C-N), 1270 (C-O), 750, 746 (=C-H). ^{1}H-NMR ($CDCl_3$, δ, ppm): 3.4 (s, 2H, CH_2- thiolactam), 7.2–7.3 (m, 8H, Ar-H), 8.7 (s, 1H, Ar-H, H-4), 11.3 (s, 1H, CH-Ar). ^{13}C-NMR ($CDCl_3$, δ, ppm): 33.5 (C_2), 64.3 (C_5), 121.5 (C_{24}), 122.2 (C_{22}), 125.5 (C_{26}), 126.8 (C_{27}), 128.4 (C_{25}), 128.7 (C_{14}), 128.7 (C_{16}), 129.4 (C_{18}), 130.1 (C_{13}), 130.1 (C_{17}), 132.7 (C_{15}), 137.3 (C_{12}), 146 (C_{23}), 150.1 (C_{21}), 161.9 (C_{19}), 171.2 (C_3). MS (m/z): 425 (M^+). Analysis: for $C_{20}H_{12}ClN_3O_4S$ calcd. C 56.41, H 2.84, N 9.87, S 7.53%; found: C 56.51, H 2.82, N 9.86, S 7.54%.

3-[5-(2-Oxo-2*H*-chromen-3-yl)-1,3,4-oxadiazol-2-yl]-2-phenyl-1,3-thiazolidin-4-one **(5m)**

Yield: 70%; m.p. 210–212°C; R_f 0.68; IR (KBr, cm^{-1}): 3220 (C-H), 2700 (N=C-H), 1591 (C=O, coumarin), 1500 (C=C), 1387 (C-N), 1230 (C-O), 756 (=C-H). ^{1}H-NMR ($CDCl_3$, δ, ppm): 3.6 (s, 2H, β-thialactam ring); 7.0–8.2 (m, 9H, Ar-H), 8.8 (s, 1H, Ar-H, H-4), 11.3 (s, 1H, -CH-Ar). ^{13}C-NMR ($CDCl_3$, δ, ppm): 33.5 (C_2), 64.3 (C_5), 121.5 (C_{24}), 122.2 (C_{22}), 125.5 (C_{26}), 126.8 (C_{27}), 127.2 (C_{15}), 128.4 (C_{25}), 128.7 (C_{13}), 128.7 (C_{14}), 128.7 (C_{16}), 128.7 (C_{17}), 129.4 (C_{18}), 139.2 (C_{12}), 146 (C_{23}), 150.1 (C_{21}), 161.9 (C_{19}), 171.2 (C_3). MS (m/z): 391 (M^+). Analysis: for $C_{20}H_{13}N_3O_4S$ calcd. C 61.37, H 3.35, N 10.74, S 8.17%; found: C 61.57, H 3.36, N 10.72, S 8.17%.

Antimicrobial activity

The synthesized compounds were screened for their antibacterial activity against Gram positive *S. aureus* and Gram negative *E. coli* strains and antifungal activity against *C. albicans* by cup plate method and agar diffusion method (18). Cipro-

Table 1. Antibacterial and antifungal activity of compounds (**5a-m**).

Comp.	Diameter of zone of inhibition (mm)			% Inhibition with reference to standard		
	S. aureus	*E. coli*	*C. albicans*	*S. aureus*	*E. coli*	*C. albicans*
5a	18	10	11	72	40	55
5b	14	12	14	56	48	70
5c	12	12	13	48	48	65
5d	11	14	12	44	56	60
5e	18	15	10	72	60	50
5f	12	12	11	48	48	55
5g	14	10	17	56	40	85
5h	13	14	13	52	56	65
5i	17	12	12	68	48	60
5j	-	18	15	-	72	75
5k	-	18	15	-	72	75
5l	-	18	16	-	72	80
5m	22	22	17	88	88	85
Cip.	25	25	-	100	100	-
Ket.	-	-	20	-	-	100

Cip. = ciprofloxacin, Ket. = ketoconazole

floxacin and ketoconazole were used as standards. The test compounds and standards were evaluated at 100 µg/mL conc. DMF was used as solvent and control. Data are represented as % inhibition with reference to standard in Table 1.

RESULTS

Salicylaldehyde and diethylmalonate were reacted in the presence of piperidine in ethanol to form ethyl-2-oxo-2*H*-chromene-3-carboxylate **1**, which on treatment with hydrazine hydrate 99% yielded 2-oxo-2*H*-chromene-3-carbohydrazide **2**. Compound **2** was warmed at 55–60°C with cyanogen bromide to form 3-(5-amino-1,3,4-oxadiazole-2-yl)-2*H*-chromen-2-one **3**. This compound was condensed with appropriate aldehydes to furnish the Schiff bases (**4a-m**), which in the presence of thioglycolic acid and a pinch of anhydrous zinc chloride were cyclized to desired 1,3-thiazolidin-4-ones (**5a-m**). The synthesized compounds were characterized by elemental analysis, IR, ^{1}H NMR, ^{13}C NMR and mass spectroscopy. The FT IR spectra revealed the following bands for C-H, N=CH, C=O (coumarin), C-N, C-O groups at 3398–3000, 2720–2700, 1717–1580, 1500–1480, 1390–1350 and 1275–1220 cm^{-1}, respectively. The ^{1}H NMR spectra confirm the presence of aromatic protons at δ 6.9–8.9 ppm. The singlet for two protons of β-thialactam ring appears at δ 3.2–3.8 ppm. Another singlet also appears for a single proton (S-CH-Ar) at δ 11.2–11.3 ppm.

It has been observed that most of the compounds showed inhibition against *S. aureus*, *E. coli* and *C. albicans*. Compounds **5a**, **5e** and **5m** showed 72%, 72% and 88% inhibition, respectively, against *S. aureus,* compounds **5j**, **5k 5l** and **5m** showed 72%, 72%, 72% and 88% inhibition, respectively against *E. coli*. and compounds **5g**, **5l** and **5m** showed 85%, 80% and 85% inhibition, respectively, against *C. albicans*.

The compounds with 2-nitro/3-nitro substitution (**5a, 5e**) and without substitution (**5m**) of the distal phenyl ring, which is attached to the thiazolidinone moiety, showed the highest *in vitro* growth inhibition against *S. aureus*, whereas the compounds with 2-chloro/3-chloro/4-chloro substitution and without substitution of the phenyl ring, showed the highest *in vitro* growth inhibition against *E. coli*. The compounds with 4-dimethylamino, 4-chloro and without substitution of the phenyl ring, showed the highest *in vitro* growth inhibition against *C. albicans*.

It can be concluded from this study that unsubstituted compound (**5m**) showed the highest *in vitro* growth inhibition against *S. aureus*, *E. coli* and *C. albicans*.

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