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Synthesis and *In-vitro* Activity of Some New Class of Thiazolidinone and Their Arylidene Derivatives

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In an attempt to find a new class of *anti* microbial agents, a series of thiazolidinone and their 5-arylidene derivatives containing 4-(4-methyl benzamido)-benzoyl moiety were synthesized *via* the reaction of benzocaine with appropriate chemical reagents. These compounds were screened for their antibacterial activity against Gram-positive bacteria (*Bacillus subtilis* and *Bacillus thuringiensis*), Gram-negative bacteria (*Escherichia coli*, *Pseudomonas aeruginosa*) and antifungal activity against *Botrytis fabae*, *Fusarium oxysporan* and *Candida albicans*. On the other hand the synthesized compounds were also screened for their *anti* tubercular activity. IR, ^{1}H NMR, ^{13}C NMR and MS spectral analyses established the structures of the newly synthesized compounds. The results revealed that some of these compounds have shown promising antimicrobial and *anti* tubercular activity in comparison with standard drugs.

Key Words : Benzocaine, *p*-Methylbenzoyl chloride, Thiazolidinone, Antimicrobial activity, *Anti* tuberculosis activity

Introduction

One of the major objectives of organic and medicinal chemistry is the design, synthesis and production of molecules, which are having highly therapeutic nature. The rapidly increasing resistance of pathogenic bacteria towards available antibiotics is a worldwide problem, as well as fungal infections continue to increase rapidly in the number of immuno compromised patients. So, the design of new molecules to deal with resistant bacteria and fungi has become one of the most important areas of antimicrobial research today.

Since the discovery of heterocyclic nucleus the chemistry of thiazolidinones and their allied compounds continue to draw attention of organic chemists due to their various biological activities such as antibacterial,[1-4] anticancer,[5] antitubercular,[6,7] antifungal,[8] *anti*-inflammatory,[9] antiviral,[10] analgesic.[11] Thiazolidinone and their arylidene derivatives are also having highly therapeutic nature such as antioxidants,[12] antitumor agents,[13] agricultural fungicides.[14]

In view of these above findings it was thought of interest to synthesize some new thiazolidinone and their chalcone derivatives having benzoyl moiety by conventional methods. In this present work we report the synthesis and anti microbial studies of (*Z*)-*N*-(5-(substitutedbenzylidene)-4-oxo-2-phenylthiazolidin-3-yl)-4-(4-methylbenzamido)benzamide derivatives.

Experimental

All melting points were measured on open capillary method. IR spectra were recorded for KBr disc on Schimadzu-8400 FT IR spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra were measured on a Bruker Avance II 400 spectrometer, operating at 400, 100.6 MHz respectively. Chemical shifts (δ) are reported in ppm and TMS as an internal standard. Reactions were monitored by thin layer chromatography (TLC) on silica gel, plates were visualizing with ultraviolet light (or) iodine. Column chromatography was performed on Merck silica gel 60 (0.043-0.060 mm).

General Procedure for the Synthesis of 4-(4-methylbenzoylamino)-benzoic Acid Ethyl Ester (1). To a solution of benzocaine (0.0l mol) in dry ether (50 mL), *p*-methyl benzoyl chloride (0.0l mol) was added drop by drop at 0 °C. The reaction mixture was stirred for 4 h, the resulting solid was filtered, dried and recrystallised to obtain compound (**1**).

IR (KBr, ν_{max}, cm^{-1}) 3340.68 (N-H), 3055.35 (C-H in hetero aromatic ring), 3042.89 (Ar-H), 2943.18 (C-H in CH_3), 2907.16 (C-H in CH_2), 1639.71 (C=O in ester), 1307.73 (C-N); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.72 (m, 8H, Ar-H), 8.12 (s, 1H, -CONH), 1.40 (t, 3H, J = 7.0 Hz, CH_3), 3.85 (q, 2H, J = 6.5 Hz, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.7 (C=O), 165.1 (C=O), 126.5, 129.1, 129.8, 131.9, 142.2 (aromatics), 25.3 (CH_3).

General Procedure for the Synthesis of *N*-(4-hydrazinocarbonyl-phenyl)-4-methyl-benzamide (2). Compound **1** (0.01 mol) and hydrazine hydrate (0.02 mol) in ethanol (20 mL) was refluxed for about 5 h on a steam bath. After cooling the resulting solid was filtered, dried and recrystallized to obtain compound **2**. Pinkish white solid, yield: 75%, mp 195-198 °C; IR (KBr, ν_{max}, cm^{-1}), 3311, 3369 (-NHNH$_2$), 3042.81 (Ar-H), 2942.16 (CH_3), 1661.73 (C=O of amide), ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.90 (s, 2H, -NH$_2$), 7.35-7.81 (m, 8H, Ar-H), 7.91 (s, 1H, -CONH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.4 (CH_3), 165.2, 169.1 (C=O), 119.8, 126.8, 131.1, 139.8 (aromatics).

General Procedure for the Synthesis of *N*-[4-(benzylidenehydrazinocarbonyl)phenyl]-4-methyl-benzamide (3). A mixture of compound **2** (0.01 mol), benzaldehyde (0.01 mol) and 2,3-drops of glacial acetic acid in ethanol (20 mL) was refluxed on a water bath for about 6 h. The solvent was removed and the residue recrystallized from chloroform-methanol mixture to yield the required compound (**3**). Brown solid, yield: 72%, mp 210-212 °C, IR (KBr, ν_{max}, cm^{-1}); 3341.72 (N-H), 3042.16 (Ar-H), 2942.16 (CH of CH_3), 1651.8 (C=O of amide), 1526.19 (C=N), 1307.73 (C-N); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.01-7.8 (m, 13H, Ar-H), 8.03 (s, 1H, CONH), 5.91 (s, 1H, =CH), 3.25 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.6 (C=O), 64.8 (=CH), 26.4 (CH_3), 119.8, 127.5, 128.8, 130.2, 140.5 (aromatics).

4-Methyl-*N*-(4-((4-oxo-2-phenylthiazolidin-3-yl)carbamoyl)phenyl)benzamide (4). To a solution of compound **3** (0.005 mol) in DMF (15 mL) was added mercapto acetic acid (0.005 mol) and $ZnCl_2$ (0.5 g) and the reaction mixture was refluxed for 8h, cooled and poured in to crushed ice, the separate solid was filtered and washed with 10% $NaHCO_3$. The crude product was dried and recrystallized from DMF to obtain the desired compound (**4**). Pale yellow crystals, yield: 75.66%; mp 230-232 °C; IR (KBr, ν_{max}, cm^{-1}); 3341.98 (N-H), 3046.19 (Ar-H), 2948.06 (CH_3), 2914.93 (C-H in CH_2), 1640.0 (ring C=O), 1628.71 (C=O of amide), 681.72 (C-S); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.60 (s, 2H, -CH_2 in ring), 3.70 (d, 1H, J = 15.8 Hz, CH-Ar), 7.01-7.71 (m, 13H, Ar-H), 8.08 (s, 1H, -CONH), 3.25 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.63 (ring S-CH_2), 54.98 (-CH), 119.8, 128.4, 129.9, 130.5, 141.8 (aromatics), 163.18 (amide-C=O), 172.35 (ring-C=O).

(*Z*)-*N*-(5-(Substitutedbenzylidene)-4-oxo-2-phenylthiazolidin-3-yl)-4-(4-methylbenzamido) benzamide (5). A mixture of compound **4** (0.005 mol), respective aldehyde (0.005 mol) and anhydrous CH_3COONa (0.005 mol) in anhydrous glacial acetic acid (50 mL) was refluxed for 3 h. The reaction mixture was concentrated and then poured into ice-cold water. The solid thus separated was filtered, washed with water and crystallized from glacial acetic acid to obtain the desired Compound. Dark yellow needles; yield: 52.2%, 245-47 °C. The compounds **5a-j** were prepared similarly by treating with corresponding aldehydes.

(*Z*)-*N*-(5-(Benzylidene)-4-oxo-2-phenylthiazolidin-3-yl)-4-(4-methylbenzamido)benzamide (5a): Dark yellow needles, yield: 52.21%, mp 245-247 °C, IR (KBr, ν_{max}, cm^{-1}) 3341.98 (N-H), 3046.27 (Ar-H), 2956.81 (CH_3), 1685.43 (C=O in ring), 1630.12 (C=O of amide), 703.29 (C-S); ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.25 (s, 3H, CH_3), 7.06-7.75 (m, 18H, Ar-H), 8.08 (s, 1H, -CONH), 7.91 (s, 1H, CH=C); ^{13}C NMR (100 MHz, DMSO-d_6) δ 25.71 (CH_3), 60.28 (-CH), 48.51 (C_5 in thiazolidinone ring), 54.9 (=CH), 117.3, 121.0, 125.2, 130.8, 140.9, 141.5 (aromatics), 163.18 (amide-C=O), 159.2 (ring-C=O); MS: *m*/*z* 520.72 [*M*+1].

(*Z*)-*N*-(5-(2-Chlorobenzylidene)-4-oxo-2-phenylthiazolidin-3-yl)-4-(4-methylbenzamido) benzamide (5b): Dark yellow needles; yield: 62.3%; mp 250-254 °C; IR (KBr, ν_{max}, cm^{-1}); 3329.11 (N-H), 3053.21 (C-H in ring), 3009.23 (Ar-H), 2956.53 (CH_3), 16835.04 (C=O in ring), 1639.21 (C=O), 1398.56 (C-N), 1087.6 (C-Cl); ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.19 (s, 3H CH_3), 7.06-7.8 (m, 17H, Ar-H); 7.98 (s, 2H, CONH), 7.91 (s, 1H, C=CH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 29.15 (CH_3), 62.51 (-CH), 50.03 (C_5 in thiazolidinone ring), 54.9 (=CH), 117.3, 121.8, 125.2, 130.8, 135.1, 140.2, 141.5 (aromatics), 162.21 (C=O), 160.92 (C=O in ring); MS: *m*/*z* 555.91 [*M*+2].

(*Z*)-*N*-(5-(4-Methoxybenzylidene)-4-oxo-2-phenylthiazolidin-3-yl)-4-(4-methylbenzamido) benzamide (5c): Dark yellow needles; yield: 58.4%; mp 241-244 °C; IR (KBr, ν_{max}, cm^{-1}); 3341.02 (N-H), 3009.23 (Ar-H), 2943.56 (CH_3), 1681.28 (C=O in ring), 1639.21 (C=O), 1398.56 (C-N), 1260.34 (C-O-C); ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.25 (s, 3H, CH_3), 3.91 (s, 3H, OCH_3), 7.10-7.78 (m, 17H, Ar-H), 7.85 (s, 1H, CH=C), 7.98 (s, 2H, CONH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 30.06 (CH_3), 62.51 (-CH), 52.19 (C_5 in thiazolidinone ring), 56.02 (=CH), 116.3, 123, 129.73, 131.4, 140.2, 158.2 (aromatics), 163.18 (C=O), 159.08 (C=O in ring); MS: *m*/*z* 550.41 [*M*+1].

(*Z*)-4-Methyl-*N*-(4-((5-(2-nitrobenzylidene)-4-oxo-2-phenylthiazolidin-3-yl)carbamoyl)phenyl)benzamide (5d): Dark yellow needles; yield: 61.2%; mp 251-254 °C; IR (KBr, ν_{max}, cm^{-1}); 3341.02 (N-H), 3009.23 (C-H in Ar), 2956.15 (CH_3), 1689.43 (C=O in ring), 1641.19 (C=O), 1525.61 (N-O), 1399.61 (C-N), 701.22 (C-S); ^{1}H NMR(400 MHz, DMSO-d_6) δ 8.11 (s, 2H, O=C-N-H), 7.93 (s, 1H, =CH), 7.78 (d, J = 8.3 Hz, 2H, Ar-H near NO_2), 7.5 (d, J = 8.6 Hz, 4H, Ar-H), 6.91-7.34 (m, 11H, Ar-H), 5.19 (s, 1H, N-CH-Ar), 2.78 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ 40.09 (CH_3), 64.28 (-CH), 52.19 (C_5 in thiazolidinone ring), 58.18 (=CH), 129.7, 134.1, 138.7, 147.12 (aromatics), 158.6 (C=O in ring), 161.3 (C=O); MS: *m*/*z* 565.48 [*M*+1].

(*Z*)-4-Methyl-*N*-(4-((4-oxo-2-phenyl-5-(3,4,5-trimethoxybenzylidene)thiazolidin-3-yl)carbamoyl)phenyl)benzamide (5e): Dark yellow needles; yield: 59.8%; mp 221-223 °C; IR (KBr, ν_{max}, cm^{-1}); 3341.07 (N-H), 3006.13 (Ar), 2949.31 (CH_3), 1681.68 (C=O in ring), 1640.21 (C=O), 1272.49 (C-O-C), 1400.11 (C-N); ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.13 (s, 2H, O=C-N-H), 7.88 (s, 1H, =CH), 7.09-7.53 (m, 13H, Ar-H), 6.89 (d, J = 9.1 Hz, 2H, Ar-H near OCH_3), 5.27 (s, 1H, N-CH-Ar), 3.46 (s, 6H, OCH_3), 3.19 (s, 3H, OCH_3), 2.42 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ 40.09 (CH_3), 52.19 (C_5 in thiazolidinone ring), 58.18 (=CH), 59.9 (OCH_3), 64.28 (-CH), 107.6, 119.2, 129.7, 134.1, 138.7, 147.12 (aromatics), 158.6 (C=O in ring), 161.3 (C=O); MS: *m*/*z* 610.24 [*M*+1].

(*Z*)-*N*-(5-(4-(Dimethylamino)benzylidene)-4-oxo-2-phenylthiazolidin-3-yl)-4-(4-methylbenzamido) benzamide (5f): Dark yellow needles; yield: 63.4%; mp 249-251 °C; IR (KBr, ν_{max}, cm^{-1}); 3341.16 (N-H), 3055.01 (C-H in ring), 3009.27 (Ar), 2956.67 (CH_3), 2932.72 (CH_3), 1691.01 (C=O in ring), 1640.03 (C=O), 1338.27 (C-N); ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.78 (s, 6H, CH_3), 2.91 (s, 3H, CH_3), 7.08-7.75 (m, 17H, Ar-H), 7.86 (s, 1H, CH=C), 7.98 (s, 2H, CONH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 40.09 (CH_3),

64.28 (-CH), 52.19 (C_5 in thiazolidinone ring), 58.18 (=CH), 114.8, 121.6, 129.8, 143.1, 150.02 (aromatics), 159.4 (C=O in ring), 164.1 (C=O); MS: *m*/*z* 563.39 [*M*+1].

(*Z*)-*N*-(5-(4-Chlorobenzylidene)-4-oxo-2-phenylthiazolidin-3-yl)-4-(4-methylbenzamido) benzamide (5g): Dark yellow needles; yield: 60.8%; mp 251-253 °C; IR (KBr, ν_{max}, cm^{-1}) 3321.23 (N-H), 3057.29 (C-H in ring), 3010.75 (Ar-H), 2951.93 (CH_3), 1690.11 (C=O in ring), 1636.84 (C=O), 1392.12 (C-N), 1093.18 (C-Cl), 701.88 (C-S); ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.19 (s, 3H, CH_3), 7.06-7.8 (m, 17H, Ar-H); 8.14 (s, 2H, CONH), 7.94 (s, 1H, C=CH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 29.15 (CH_3), 62.51 (-CH), 50.03 (C_5 in thiazolidinone ring), 54.9 (=CH), 117.3, 121.8, 125.2, 130.8, 135.1, 140.2, 141.5 (aromatics), 162.21 (C=O), 160.92 (C=O in ring); MS: *m*/*z* 555.93 [*M*+2].

(*Z*)-4-Methyl-*N*-(4-((5-(4-methylbenzylidene)-4-oxo-2-phenylthiazolidin-3-yl)carbamoyl)phenyl)benzamide (5h): Dark yellow needles; yield: 59.2%; mp 249-250 °C; IR (KBr, ν_{max}, cm^{-1}); 3297.55 (N-H), 3052.11 (C-H in ring), 3027.18 (Ar), 2955.12 (CH_3), 2949.16 (CH_3), 1683.09 (C=O in ring), 1643.12 (C=O), 1399.29 (C-N), 701.82 (C-S); ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.92 (s, 6H, CH_3), 7.08-7.8 (m, 17H, Ar-H), 7.82 (s, 1H, CH=C), 7.94 (s, 2H, CONH); ^{13}C NMR (100 MHz, DMSO-d_6) δ 40.09 (CH_3), 64.28 (-CH), 52.19 (C_5 in thiazolidinone ring), 58.18 (=CH), 114.8, 121.6, 129.8, 143.1, 150.02 (aromatics); MS: *m*/*z* 534.41 [*M*+1].

(*Z*)-4-Methyl-*N*-(4-((5-(4-nitrobenzylidene)-4-oxo-2-phenylthiazolidin-3-yl)carbamoyl)phenyl)benzamide (5i): Dark yellow needles; yield: 59.9%; mp 249-251 °C; IR (KBr, ν_{max}, cm^{-1}); 3341.02 (N-H), 3009.91 (C-H in Ar), 2954.78 (CH_3), 1679.28 (C=O in ring), 1641.19 (C=O), 1525.61 (N-O), 1399.61 (C-N), 701.22 (C-S); ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.11 (s, 2H, O=C-N-H), 7.93 (s, 1H, =CH), 7.71 (d, *J* = 8.3 Hz, 2H, Ar-H near NO_2), 7.5 (d, *J* = 8.3 Hz, 4H, Ar-H), 6.91-7.35 (m, 11H, Ar-H), 5.19 (s, 1H, N-CH-Ar), 2.73 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ 40.09 (CH_3), 64.28 (-CH), 52.19 (C_5 in thiazolidinone ring), 58.18 (=CH), 129.1, 133.5, 138.7, 147.12 (aromatics), 158.6 (C=O in ring), 162.1 (C=O). MS: *m*/*z* 565.48 [*M*+1].

(*Z*)-*N*-(5-(4-Bromobenzylidene)-4-oxo-2-phenylthiazolidin-3-yl)-4-(4-methylbenzamido) benzamide (5j): Dark yellow needles; yield: 57.2%; mp 238-241 °C; IR (KBr, ν_{max}, cm^{-1}); 3341.02 (N-H), 3009.91 (C-H in Ar), 2952.54 (CH_3), 1685.27 (C=O in ring), 1641.19 (C=O), 1399.61 (C-N), 701.22 (C-S). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.02 (s, 2H, O=C-N-H), 7.93 (s, 1H, =CH), 7.5 (d, *J* = 8.6 Hz, 4H, Ar-H), 6.91-7.59 (m, 13H, Ar-H), 5.13 (s, 1H, N-CH-Ar), 2.85 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ 40.09 (CH_3), 64.28 (-CH), 52.19 (C_5 in thiazolidinone ring), 58.18 (=CH), 128.2, 129.1, 133.5, 138.7 (aromatics), 157.2 (C=O in ring), 163.4 (C=O). MS: *m*/*z* 600.12 [*M*+1].

Antimicrobial Studies Procedure. The newly prepared compounds **5a-j** were screened for their *anti* microbial activity against *Bacillus subtilis*, *Bacillus thuringiensis*, *Escherichia coli* and *Pseudomonas aeruginosa* bacterial strains and *Candida albicans*, *Botrytis fabae* and *Fusarium oxysporam* fungal strains were used This activity was determined by agar diffusion method. Compounds were dissolved in DMSO at concentration 1 mg mL^{-1}.

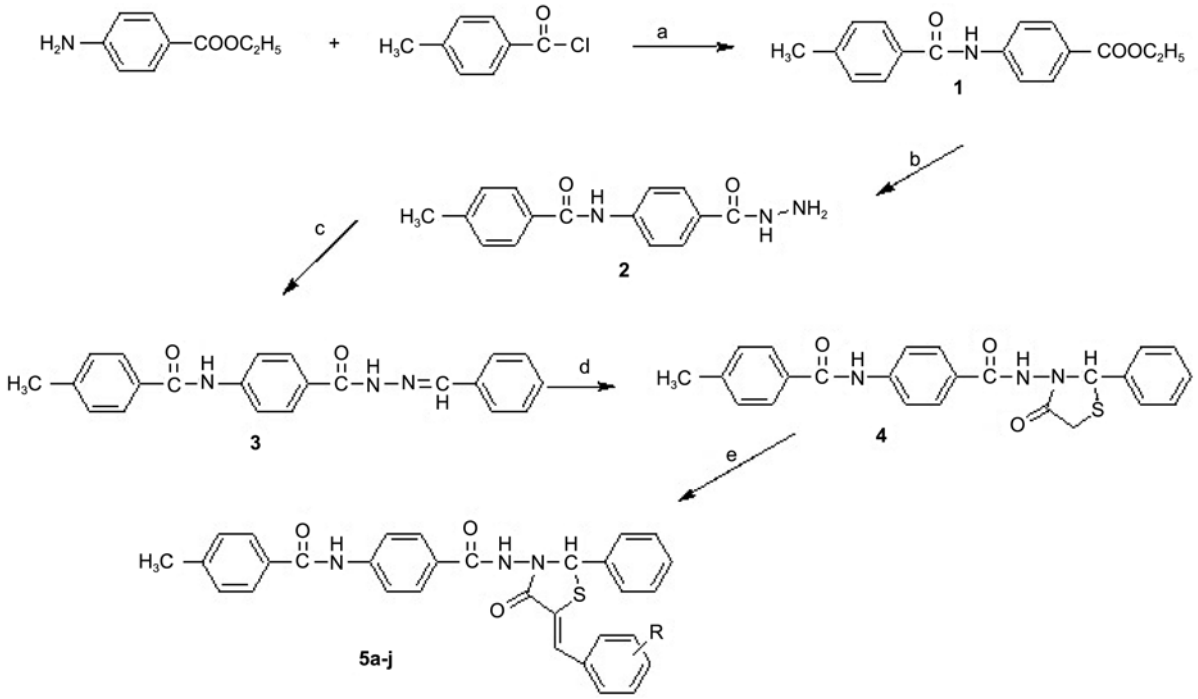
The antibacterial and antifungal activities of each compound were compared with Streptomycin and Treflucan as the standard drugs.

The results were recorded for each tested compound as the average diameter of inhibition zones (IZ) of bacterial or fungal growth around the disks in mm. The minimum inhibitory concentration (MIC) measurement was showed significant growth inhibition zones (> 10 mm) using twofold serial dilution method.

Anti Tubercular Studies Procedure. All the synthesized compounds of series **5a-j** were evaluated for their *anti* tubercular activity. Drug susceptibility and determination of MIC of the test compounds against *M. tuberculosis* H37Rv were performed by agar micro dilution method, where two fold dilutions of each test compound were added into 7H10 agars supplemented with OADC and organism. A culture of used microorganism *M. tuberculosis* H37Rv growing on L-J medium was harvested in 0.85% saline with 0.05% Tween-80. A suspension of compounds was prepared in DMSO. This suspension was added to (in tubes) 7H10 middle brook's medium (containing 1.7 mL medium and 0.2 mL OADC supplement) at different concentrations of compound keeping the volume constant, that is, 0.1 mL medium was allowed to cool keeping the tubes in slanting position. These tubes were then incubated at 37 °C for 24 h followed by streaking of *M. tuberculosis* H37Rv (5×10^4 bacilli per tube). These tubes were then incubated at 37 °C. Growth of bacilli was seen after 30 days of incubation. Tubes having the compounds were controlled with control tubes where medium alone was incubated with H37Rv. The concentration at which complete inhibition of colonies occurred was taken as active concentration of test compound. Isoniazid was used as standard drug. The MIC levels of some active compounds **5a-j** against these organisms were given in Table 2.

Results and Discussion

Chemistry. In the present work, a series of new moieties was synthesized. Scheme 1 describes the path used for the preparation of target compounds. The key intermediate, 4 required for the synthesis of title compounds was prepared according to the procedure outlined in the Scheme 1. For the synthesis of required reaction sequence including benzoylation of benzocaine at the first step, which involves the protection of the amino function gave 4-(4-Methyl-benzoyl-amino)-benzoic acid ethyl ester (1). Hydrazinolysis of compound **1** then gave *N*-(4-hydrazinocarbonyl-phenyl)-4-methyl-benzamide (2). This was later reacted with benzaldehyde in the presence of glacial. AcOH in methanol at reflux temperature gave 4-(Benzylidene-hydrazino[*N*-4-methyl-benzamide]Carbonyl)-phenyl (3). Compound **3** was then reacted with thioglycolic acid in the presence of anhydrous $ZnCl_2$ under conventional heating conditions (Scheme 1) to give compound **4**. Compound **4** was reacted with various aromatic aldehydes in the presence of anhydr-



5a R=H, **5b** R=2-Cl, **5c** R=4-OH, **5d** R=2-NO_2, **5e** R=3,4,5-$(OCH_3)_3$, **5f** R=4-$N(CH_3)_2$, **5g** R=4-Cl, **5h** R=4-CH_3, **5i** R=4-NO_2, **5j** R=4-Br

Scheme 1. Synthesis of compounds **5a-j**.
Reaction conditions: a) Dry ether, 0 °C, b) $NH_2NH_2{\cdot}H_2O$, ethanol, c) Benzaldehyde, glacial AcOH, d) $SHCH_2COOH$, DMF, anhydrous $ZnCl_2$, e) aromatic aldehydes, anhydrous CH_3COONa, glacial AcOH.

ous NaOAc in glacial acetic acid at reflux temperature to give chalcone derivatives of thiazolidinones 5. The structures of the synthesized compounds were confirmed by IR, ^{1}H NMR, ^{13}C NMR and mass spectral analysis.

In the IR spectra of compounds **5a-j** disappearance of active methylene group absorption band at 2914.73 cm^{-1}, which was present in compound **4**, confirmed the chalcone derivatives of Thiazolidinone system.

In the ^{1}H NMR spectra of compounds **5a-j**, recorded in DMSO-d_6, The disappearance of active methylene group signal at 4.03 ppm as a singlet, which was present in compound **4**, as well as the appearance of various signals due to =CH protons appeared at 7.9 ppm as a singlet and the N-CH-S proton of thiazolidinone ring at 5.51-5.65 ppm as a singlet demonstrate that the condensation step had occurred. All the other aromatic protons of **5a-j** were observed at the expected regions. In the ^{13}C NMR spectrum of compounds **5a-j**, recovered in DMSO-d_6, the prominent signals corresponding to the carbons of chalcone derivatives of thiazolidinone moiety observed nearly at 25.71, 48.51, 54.9, 60.28,

Table 1. *Anti* bacterial and *anti* fungal data of compounds **5a-j**

Compound No.	Bacteria[b]				Fungi[c]		
	B. subtilis	*B. thuringiensis*	*E. coli*	*P. aeruginosa*	*B. fabae*	*F. oxysporam*	*C. albicans*
5a	12.5	12.5	12.5	25	25	25	12.5
5b	3.125	3.125	6.25	6.25	12.5	12.5	6.25
5c	25	25	25	50	6.25	3.125	3.125
5d	3.125	3.125	3.125	3.125	25	25	25
5e	25	NA[a]	NA[a]	25	3.125	3.125	3.125
5f	6.25	12.5	12.5	NA[a]	12.5	12.5	25
5g	3.125	3.125	3.125	6.25	25	NA[a]	12.5
5h	25	25	NA[a]	NA[a]	3.125	6.25	3.125
5i	3.125	3.125	6.25	6.25	12.5	6.25	6.25
5j	6.25	6.25	6.25	6.25	NA[a]	25	12.5
Strepto mycin	3.125	6.25	6.25	6.25	NA[a]	NA[a]	NA[a]
Treflucan	NA[a]	NA[a]	NA[a]	NA[a]	3.125	3.125	3.125

[a]Not Active. [b]*B. subtilis* (MTCC No: 1133), *B. thuringiensis* (MTCC No: 4714), *E. coli* (MTCC No: 443), and *P. aeruginosa* (MTCC No: 2297). [c]*B. fabae* (ATCC No: 14862), *F. oxysporam* (MTCC No: 7392) and *C. albicans* (MTCC No: 183)

130.8, 167.18 and 171.72 ppm are proof of further evidence of their structures.

Pharmacology.

Anti Microbial Studies: The results depicted in Table 1 revealed that most of tested compounds displayed variable inhibitory effects on the growth of tested gram positive, gram negative bacterial strains and fungal strains.

The *anti* bacterial screening data showed moderate activity of the test compounds. Among the screened **5b**, **5d**, **5g**, **5i** and **5j** in which chalcone derivatives of thiazolidinones bearing *o*-chlorophenyl, *o*-nitrophenyl, *p*-chlorophenyl, *p*-nitrophenyl and *p*-bromophenyl nucleus respectively show high activity due to the presence of benzoyl moiety against all the microorganisms employed. In this view compound **5b** and **5i** were equipotent to streptomycin against *B. subtilis* (MIC, 3.125 μg/mL), *E. coli* (MIC, 6.25 μg/mL) and *P. aeruginosa* (MIC, 6.25 μg/mL), while its activity was more potent to streptomycin against *B. thuringiensis* (MIC, 3.125 μg/mL). In the same way compound **5d** was more potent than streptomycin against all the strains employed except *B. subtilis*. Besides this compound **5g** was equipotent to streptomycin against *B. subtilis* (MIC, 3.125 μg/mL) and *P. aeruginosa* (MIC, 6.25 μg/mL), while its activity was 50% more potent to streptomycin against all other bacterial strains employed (MIC, 3.125 μg/mL) and the compound **5j** was equipotent to streptomycin against all the strains employed except *B. subtilis* (MIC, 6.25 μg/mL). Finally the activity of these compounds showed moderate to good antibacterial activity.

Regarding the activity of thiazolidinones and their 5-arylidenes derivatives incorporating benzoyl moiety against antifungal strains the results revealed that compounds **5c**, **5e**, **5h** and **5i** revealed strong growth inhibitory against the tested fungi. In this view compound **5c** was equipotent to treflucan against *F. oxysporam* and *C. albicans* (MIC, 3.125 μg/mL), while its activity was 50% less potent to treflucan against *B. fabae* (MIC, 6.25 μg/mL). And compound **5e** was equipotent to treflucan against all the strains employed (MIC, 3.125 μg/mL). On the other hand 5 h was equipotent to treflucan against *B. fabae* and *C. albicans* (MIC, 3.125 μg/mL), while its activity was 50% less potent to treflucan against *F. oxysporam* (MIC, 6.25 μg/mL). Finally the activity of these compounds showed moderate to good antifungal activity.

Table 2. *Anti* tubercular activity data of compounds **5a-j**

Compound	MIC (μg/mL)
5a	> 25
5b	> 3.125
5c	> 25
5d	6.25
5e	> 25
5f	> 12.5
5g	> 6.25
5h	> 12.5
5i	> 3.125
5j	6.25
Streptomycin	4.0

Anti Tubercular Studies: The results depicted in Table 2 revealed that most of the tested compounds, displayed variable inhibitory effects on the growth of the tested *M. tuberculosis* H37Rv strains.

Generally compounds possessing electron-withdrawing groups showed good *anti* tubercular activity. Some derivatives (**5b**, **5d**, **5g**, **5i** and **5j**) containing electron-withdrawing groups (-Cl, -NO_2, -Br) have shown promising activity against M. tuberculosis.

Conclusion

In conclusion, the obtained results clearly revealed that some of the newly synthesized compounds where the benzoyl moiety attached to arylidene-substituted thiazolidinones (**5b**, **5d**, **5g** and **5i**) exhibited promising antimicrobial, *anti* tubercular activity.

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References

1. Khan, S. A.; Yousuf, M. *Eur. J. Med. Chem.* **2009**, *44*, 2597.
2. Palekar, V. S.; Damle, A. J.; Shukla, S. R. *Eur. J. Med. Chem.* **2009**, *44*, 5112.
3. Kucukguzel, S. G.; Oruc, E. E.; Rollas, S.; Sahin, F.; Ozbek, A. *Eur. J. Med. Chem.* **2002**, *37*, 197.
4. Bonde, C. G.; Gaikwad, N. J. *Bioorg. Med. Chem.* **2004**, *12*, 2151.
5. Bhatt, J. J.; Shah, B. R.; Shah, H. P.; Trivedi, P. B.; Undavia, N. K.; Desai, N. C. *Ind. J. Chem.* **1994**, *33B*, 189.
6. Babaoglu, K.; Page, M. A.; Jones, V. C.; Mc Neil, M. R.; Dong, C.; Naismith, J. H.; Lee, R. E. *Bioorg. Med. Chem. Lett.* **2003**, *13*, 3227.
7. Ulusoy, N. *Forsch, A. Drug Res.* **2002**, *52*, 565.
8. Hogale, M.; Uthale, A. *Proc. Ind. Acad. Sci.* **1990**, *102*, 535.
9. Yadav, R.; Srivastava, S. D.; Srivastava, S. K. *Ind. J. Chem.* **2005**, *44B*, 1262.
10. Barreca, M. L.; Chimirri, A.; Luca, L. D.; Monforte, A. M.; Monforte, P.; Rao, A.; Jappala, M.; Balzarini, J.; Clercq, E. De.; Pannecouque, C.; Witvrouw, M. *Bioorg. Med. Chem. Lett.* **2001**, *11*, 1793.
11. Vigorita, M. G.; Ottana, R.; Monforte, F.; Maccari, R.; Trovato, A.; Monforte, M. T.; Taviano, M. F. *Bioorg. Med. Chem. Lett.* **2001**, *11*, 2791.
12. Abdel-Wahab, B. F.; Awad, G. E. A.; Badria, F. A. *Eur. J. Med. Chem.* **2011**, *46*, 1505.
13. Havrylyuk, D.; Mosula, L.; Zimenkovsky, B.; Vasylenko, O.; Gzella, A.; Lesyk, R. *Eur. J. Med. Chem.* **2010**, *45*, 5012.
14. Lakhan, R.; Singh, R. L. *Proc. Indian Acad. Sci. (Chem. Sci.)* **1991**, *33*, 103.