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**Research Article**

# Synthesis and Antibacterial Activity of Some Newer Thiazolidine-2,4-Dione Derivatives

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**Abstract:**
Thiazolidin-2,4-diones were intensively studied for its antidiabetic property in 1982. Thiazolidin-2,4-diones have also been demonstrated to possess different biological activity like anticancer, anti-HIV, antitumor, antimicrobial, antiviral and antiproliferative activity. 3-Benzoyl-5-(substituted benzylidine)-thiazolidin-2,4-diones and 3-*p*-Tolyl-5-(substituted benzylidine)-thiazolidin-2,4-diones have evaluated as structurally novel antimicrobials. A series of 5-[(SubstitutedPhenylamino)benzylidine]thiazolidine-2,4-dione derivatives **17(a-j)** were synthesized by nucleophilic substitution reaction of (*Z*)-5-(2-Fluororobenzylidin)-thiazolidin-2,4-dione with various benzaldehyde derivatives and (*Z*)-5-(2-Fluororobenzylidin)-thiazolidin-2,4-dione were synthesized by condensation of thiazolidin-2,4-dione with *p*-fluorobenzaldehyde**.** The reaction was monitored by TLC on silica gel G plates and the final compounds were purified by recrystalization from ethanol.The structure of newly synthesized compounds **17(a-j)** were confirmed by FTIR, $^{1}$H NMR, EIMS spectral analysis and elemental analysis. All the synthesized compounds were screened for antibacterial. Antibacterial activity was screened against Gram positive (*B. subtilis, P. aeruginosa)* and Gram negative bacteria (*E.coli, S. aureus)* by paper disc diffusion method, using nutrient agar medium. The compounds substituted with hydroxyl, methoxy, nitro and chloro on aryl ring attached with thiazolidin-2,4-dione showed good antibacterial activity. The synthesized compound: **17c** and **17d** showed significant antibacterial activity against gram positive bacterial strain ***B.subtilis*** and ***S.aureus*** and compound **17g** showed significant antibacterial activity against gram negative bacterial strains ***E.coli*** and ***P.aeruginosa***. The zone of inhibition was compared with standard drugs ciprofloxacin at 50 µg/ml concentration.

## Introduction

Thiazolidine-2,4-diones are derivatives of thiazolidine with two carbonyl groups at the 2nd & 4th position (E). Substituents in the 3- and 5-positions may be varied, but significant difference in structure and properties is exerted by the group attached to the carbon atom in the 4-position by replacing oxo group and by replacing the thio group from 1-position (R in 4 position or X in 1 position). Variations in the substituents attached to the nitrogen atom are possible for the structures.

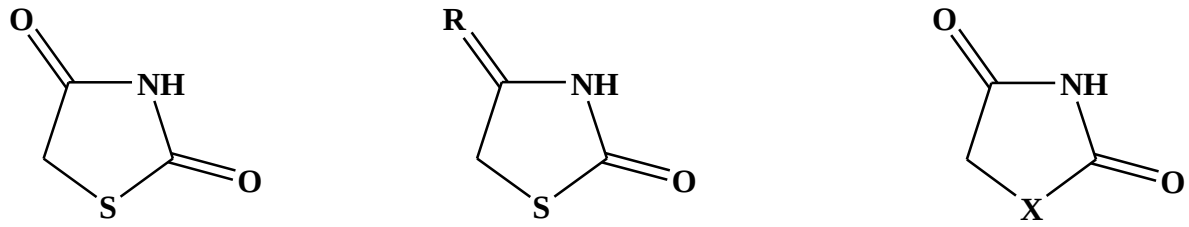



**Figure 1: Thiazolidine-2, 4-dione ring and substitutions**

Thiazolidinediones are heterocyclic ring system with multiple applications. In 1982 a number of 2, 4-Thiazolidinediones were intensively studied for their antidiabetic property. The first representative of group, Ciglitazone followed by the synthesis of the other derivatives like Englitazone, Pioglitazone and Troglitazone. All share a common thiazolidine-2, 4-dione structure which is responsible for the majority of the therapeutic activity. After this thiazolidinediones derivatives have been studied extensively and found to have diverse chemical reactivity and broad spectrum of biological activity.

As per exhaustive literature survey & data collection about the thiazolidine-2, 4-dione nucleus, it reveals that the moiety possess various biological activities namely cytotoxic, antimicrobial, anti-inflammatory, antihyperglycaemic, antiepileptic, antitubercular, anti-HIV, analgesic, anthelmintic, antiarrhythmic, antimalarial, antiparasitic, thyromimmetics, etc., but literature reviews reflects mainly on antimicrobial and cytotoxic activity. The thiazolidine ring is a frequent moiety of numerous drugs such as: butamison (antihelmintic activity), clometocillin (antibiotic activity), clospirazine (antipsychotic activity), dithiazanine (anthelmintic activity), etozoline (diuretic activity), letosteine (mucolytic activity), methicillin (antibiotic), mycobacidin (antimicrobial), pidotimod (immunomodulator), pioglitazone (antidiabetic activity), tiramide (anti-inflammatory) and timonacic (hepatoprotective). As per scientific literature review it has been found that the drugs having thiazolidine nucleus still possess some adverse effects, like; plasma volume expansion, edema, haematuria, etc. Hence there is a need to synthesize the thiazolidine analogues with lesser side effects and potent biological activities.

## Results and Discussion

### Chemistry

A series of 5-[(Substituted Phenylamino) benzylidine] thiazolidine-2,4-dione derivatives **17(a-j)** were synthesized by nucleophilic substitution reaction of (*Z*)-5-(2-Fluororobenzylidin)-thiazolidin-2,4-dione with various benzaldehyde derivatives and (*Z*)-5-(2-Fluororobenzylidin)-thiazolidin-2,4-dione were synthesized by condensation of thiazolidin-2,4-dione with *p*-fluorobenzaldehyde**.** The reaction was monitored by TLC on silica gel G plates and the final compounds were purified by recrystalization from ethanol.The structure of newly synthesized compounds **17(a-j)** were confirmed by FTIR, $^{1}$H NMR, EIMS spectral analysis and elemental analysis.

The newly synthesized compounds were identified on the basis of Rf value, melting point range, solubility studies, FTIR, 1H-NMR, 13C-NMR, MASS Spectral data and elemental analysis. The 1H-NMR spectrum showed the presence δ 6.00-7.00 was assigned to the N-H (aliphatic) proton. N-H aromatic Protons and aromatic protons at δ: 9.00-10.00 and 6.00-8.00 ppm respectively. FTIR spectrum showed the presence of characteristic peak of N-H at 3200-3450 cm-1, ketonic C=O at 1705-1720 cm-1 and C=N peak at 1500-1600 cm$^{-1}$

### Pharmacological Activity

The newly synthesized compounds were screened *in-vitro* for their antibacterial activity using disc diffusion method. The antibacterial

activities of all the synthesized compounds were carried out against the pathogenic bacterial strains ***S. aureus, B. subtilis*** (**gram positive**) and ***E. coli, P. aeruginosa*** (**gram negative**). The zone of inhibition was measured by antibiotic zone reader.

The results are shown in table 1 and 2 which revealed that the newly synthesized compounds **17d** and **17e** showed good antibacterial activity with 14.06, and 13.33mm zone of inhibition respectively against *B.subtilis* when given at concentration 50µg $ml^{-1}$ whereas under identical conditions standard drug ciprofloxacin showed 17.10mm zone of inhibition. Compounds **17i** and 1**7j** showed moderate antibacterial activity with 12.40 and 12.60mm zone of inhibition respectively against *B. subtilis.* Compounds **17d** and **17e** showed good antibacterial activity with 17.96, and 17.86mm zone of inhibition respectively against *S.aureus* when given at concentration 50µg $ml^{-1}$ whereas under identical conditions standard drug ciprofloxacin showed 21.20mm zone of inhibition. Compounds **17f** and **17h** showed moderate antibacterial activity with 16.73, 16.63mm zone of inhibition respectively against *S. aureus* when given at concentration 50µg $ml^{-1}$. Compound **17g** showed good antibacterial activity with 18.13mm zone of inhibition against *E.coli* given at concentration 50µg $ml^{-1}$ whereas under identical conditions standard drug ciprofloxacin showed 23.00mm zone of inhibition. Compounds **17d** and **17e** showed moderate antibacterial activity with 17.66 and 17.32mm zone of inhibition respectively against *E.coli*. Compound **17g** showed good antibacterial activity with 20.00mm zone of inhibition against *P. aeruginosa* when given at concentration 50µg $ml^{-1}$ where as under identical conditions standard drug ciprofloxacin showed 24.50mm zone of inhibition. Compound **17d** showed moderate antibacterial activity with 19.50mm zone of inhibition against *P. aeruginosa.*

## Experimental

## Materials and Methods

The melting points were determined in open capillary tubes and are uncorrected. The homogeneity of all the newly synthesized compounds were checked by TLC on silica gel-protected aluminum sheets (Type 60 $F_{254}$, Merck) and the spots were detected by exposure to UV-lamp at 254 nm for few seconds. The infrared (IR) spectra were recorded on 470-Shimadzu Infrared Spectrophotometer using KBr disc technique and expressed in $cm^{-1}$. $^1H$ NMR spectra were recorded on Bruker DRX-300 in DMSO-$d_6$ as a solvent. The chemical shift was given in δ (ppm) downfield from tetramethylsilane (TMS) as an internal standard. Splitting patterns were designated as follows: s: singlet; d: doublet; t: triplet; q: quartet; m: multiplet. Elemental analysis was carried on Elemental Vario EL III Carlo Erba 1108 and the values were within ±0.4% of the theoretical values.

### Procedure for the Synthesis of thiazolidine-2, 4-Dione

Equimolar quantity of chloroacetic acid (18.9 gm, 0.2 mol) and thiourea (15.2 gm, 0.2 mol) was dissolved in 20 ml of water in a three necked flask. The mixture was stirred for 15 minute to obtained white precipitate. To the content of the flask 20 ml of concentrated hydrochloric acid was added slowly from the dropping funnel, flask was then connected with condenser and gentle heat applied to complete the reaction. The mixture was stirred and refluxed for 12 hr. On cooling the content of the flask solidified to a cluster of white needles. The product was filtered, washed and recrystallized from ethanol to give desired compound. (**Yield 11.25 gm, 48.02%, m.p. 118-120°C**)

### Procedure for the Synthesis of (*Z*)-5-(2-Fluororobenzylidin)-thiazolidin-2, 4-dione

Equimolar quantity of thiazolidin-2, 4-dione (4.68gm, 0.04 mol) and *p*-fluoro benzaldehyde (4.96gm, 0.04mol) were taken and suspended in dry toluene. To this, catalytic amount of piperidine (0.5ml) was added. The reaction mixture was stirred and refluxed for 3 hours at 110°C. The compound was filtered and washed

with cold dry toluene. The compound was dried and recrystallized with ethyl alcohol to obtained intermediate product (*Z*)-5-(2-Fluororobenzylidin)-thiazolidin-2, 4-dione. (Yield 58.5%, m.p. 208-210°C).

**General Procedure for the synthesis of (Z)-5-(4-fluororobenzylidene)-3-[(9H-carbazole-9-yl) (2-chlorophenyl) methyl] thiazolidine-2,4-dione**

Equimolar quantity of (*Z*)-5-(4-fluororobenzylidin)-thiazolidin-2,4-dione (0.001mol) and carbazole (0.001mole) was dissolved in 5 ml of ethanol and *o*-chlorobenzaldehyde (0.0015mole) was added to this reaction mixture. To this 0.5 ml of concentrated HCl was added. The reaction mixture was refluxed for 11 hours with continuous stirring. The reaction mixture was filtered and cold water was added to the filtrate. The product was precipitated out, which was filtered, dried and recrystallized from ethanol to obtain the final product.

**The analytical and spectral data of final compounds are given in the following text.**

**(*Z*)-5-(4-fluororobenzylidene)-3-[(9*H*-carbazole-9-yl) (2-chlorophenyl) methyl] thiazolidine-2,4-dione (17a)**

**TLC analysis:** Solvent system: Benzene: Ethyl Acetate: Glacial Acetic Acid (9.0:0.5:0.5), $R_f$: 0.58

**Spectral data: UV $\lambda_{max}$ (DMSO):** 285.0 nm

**FTIR (KBr)(ν):** 3045.39 (Aromatic C-H str.), 1704.96 (C=O str., amide (cyclic lactums)), 1593.09 (Aromatic C=C str.), 1336.58 (C-F str.), 1153.35 (C-N str.), 916.12 (C-S str.), 815.83 (C-H def *p*-disubstituted bezene), 690.47 $cm^{-1}$ (C-Cl str.).

**$^1$H NMR (DMSO-$d_6$ ):** δ 1.620 (s, 1H, C-H), 5.274 (s, 1H, vinylic C-H), 7.104-7.132 (d, 1H, Ar-H), 7.134-7.159 (t, 1H, Ar-H), 7.161-7.182 (t, 1H, Ar-H), 7.185-7.245 (t, 1H, Ar-H), 7.247-7.272 (d, 1H, Ar-H), 7.274-7.388 (d, 1H, Ar-H) 7.390-7.508 (t, 1H, Ar-H), 7.510-7.519 (t, 1H, Ar-H) 7.521-7.558 (d, 1H, Ar-H), 7.560-7.621 (d, 1H, Ar-H), 7.625-7.642 (d, 1H, Ar-H), 7.646-7.919 (d, 1H,Ar-H), 7.921-8.023 (t, 1H, Ar-H), 8.025-8.059 (d, 1H, Ar-H), 8.061-8.223 (d, 1H, Ar-H), 8.225-8.235 ppm (d, 1H, Ar-H).

**EIMS (m/z) (%relative abundance):** $[M]^+$ 512.98 (100), [M+1] 513.04 (32), [M+2] 514.09 (26).
Fragments: 493.07 (52), 477.10 (26), 383.08 (19), 293.05 (32), 217.02 (43) 127.98 (13), 113.96 (30).

**Elemental analysis:**

Calculated for $C_{29}H_{18}ClFN_2O_2S$: C, 67.90; H, 3.54; N, 5.46; Found: C, 67.88; H, 3.56; N, 5.43%.

**(*Z*)-5-(4-fluororobenzylidene)-3-[(9*H*-carbazole-9-yl) (3-chlorophenyl) methyl] thiazolidine-2,4-dione (17b)**

**TLC analysis:**

Solvent system: Benzene: Ethyl Acetate: Glacial Acetic Acid (9.0:0.5:0.5), $R_f$: 0.61

**Spectral data:**

**UV $\lambda_{max}$ (DMSO):** 283.0 nm

**FTIR (KBr)(ν):** 3045.39 (Aromatic C-H str.), 1703.03 (C=O str., amide (cyclic lactums)), 1593.09 (Aromatic C=C str.), 1334.65 (C-F str.), 1151.42 (C-N str.), 918.05 (C-S str.), 815.62 (C-H def *p*-disubstituted bezene), 691.47 $cm^{-1}$ (C-Cl str.).

**$^1$H NMR (DMSO-$d_6$):** δ 1.624 (s, 1H, C-H), 5.261 (s, 1H, vinylic C-H), 7.104-7.132 (d, 1H, Ar-H), 7.134-7.160 (t, 1H, Ar-H), 7.161-7.182 (t, 1H, Ar-H), 7.185-7.245 (t, 1H, Ar-H), 7.247-7.272 (d, 1H, Ar-H), 7.274-7.388 (d, 1H, Ar-H) 7.390-7.508 (t, 1H, Ar-H), 7.510-7.519 (t, 1H, Ar-H) 7.521-7.558 (d, 1H, Ar-H), 7.560-7.624 (d, 1H, Ar-H), 7.625-7.642 (d, 1H, Ar-H), 7.646-7.919 (d, 1H,Ar-H), 7.921-8.021 (d, 1H, Ar-H), 8.025 (s, 1H, Ar-H), 8.064-8.243 (d, 1H, Ar-H), 8.247-8.252 ppm (d, 1H, Ar-H).

**EIMS (m/z) (% relative abundance):** $[M]^+$ 512.02 (100), [M+1] 513.10 (49), [M+2] 514.18 (43).

Fragments: 493.07 (58), 477.54 (24), 383.08 (18), 293.05 (26), 217.02 (39), 127.98 (14),

113.96 (25).

**Elemental analysis:**

Calculated for $C_{29}H_{18}ClFN_2O_2S$: C, 67.90; H, 3.54; N, 5.46;

Found: C, 67.89; H, 3.53; N, 5.42.

**(*Z*)-5-(4-fluororobenzylidene)-3-[(9*H*-carbazole-9-yl) (4-chlorophenyl) methyl] thiazolidine-2,4-dione (17c)**

**TLC analysis:** Solvent system: Benzene: Ethyl Acetate: Glacial Acetic Acid (9:0.5:0.5), $R_f$: 0.78

**Spectral data: UV $\lambda_{max}$ (DMSO):** 287.0 nm

**FTIR (KBr) (ν):** 3053.11 (Aromatic C-H str.), 1705.03 (C=O str., amide (cyclic lactums)), 1606.59 (Aromatic C=C str.), 1334.65 (C-F str.), 1153.35 (C-N str.), 914.12 (C-S str.), 814.63 (C-H def *p*-disubstituted bezene), 690.47 $cm^{-1}$ (C-Cl str.).

**$^1$H NMR (DMSO-$d_6$)** δ 1.620 (s, 1H, C-H), 5.391 (s, 1H, vinylic C-H), 7.104-7.132 (d, 1H, Ar-H), 7.134-7.160 (d, 1H, Ar-H), 7.161-7.182 (t, 1H, Ar-H), 7.185-7.245 (t, 1H, Ar-H), 7.247-7.273 (d, 1H, Ar-H), 7.274-7.387 (d, 1H, Ar-H) 7.390-7.507 (t, 1H, Ar-H), 7.510-7.518 (t, 1H, Ar-H) 7.521-7.556 (d, 1H, Ar-H), 7.560-7.623 (d, 1H, Ar-H), 7.625-7.643 (d, 1H, Ar-H), 7.646-7.918 (d, 1H,Ar-H), 7.921-8.021 (d, 1H, Ar-H), 8.025-8.059 (d, 1H, Ar-H), 8.061-8.101 (d, 1H, Ar-H), 8.103-8.121 ppm (d, 1H, Ar-H).

**EIMS (m/z) (% relative abundance):** $[M]^+$ 512.98 (100), [M+1] 513.04 (30), [M+2] 514.10 (26).

Fragments: 493.07 (58), 477.51 (28), 383.08 (19), 293.05 (30), 217.02 (40), 127.98 (13), 113.96 (30).

**Elemental analysis:**

Calculated for $C_{29}H_{18}ClFN_2O_2S$: C, 67.90; H, 3.54; N, 5.46; Found: C, 67.88; H, 3.56; N, 5.43.

**(*Z*)-5-(4-fluororobenzylidene)-3-[(9*H*-carbazole-9-yl) (3-nitrophenyl) methyl] thiazolidine-2,4-dione (17d)**

**TLC analysis:** Solvent system: Benzene: Ethyl Acetate: Glacial Acetic Acid (9.0:0.5:0.5), $R_f$: 0.85

**Spectral data: UV $\lambda_{max}$ (DMSO):** 365.0 nm

**FTIR (KBr) (ν):** 3053.11 (Aromatic C-H str.), 1704.03 (C=O str., amide (cyclic lactums)), 1606.59 (Aromatic C=C str.), 1529.45 (Asymmetric N=O str.), 1334.65 (C-F str.), 1316.26 (Symmetric N=O str.), 1166.35 (C-N str.), 917.12 (C-S str.), 800.98 $cm^{-1}$ (C-H def *p*-disubstituted bezene).

**$^1$H NMR (DMSO):** δ 1.662 (s, 1H, C-H), 5.332 (s, 1H, vinylic C-H), 6.990-7.122 (d, 1H, Ar-H), 7.125-7.145 (t, 1H, Ar-H), 7.148-7.171 (t, 1H, Ar-H), 7.173-7.212 (t, 1H, Ar-H), 7.213-7.233 (d, 1H, Ar-H), 7.236-7.293 (d, 1H, Ar-H) 7.295-7.330 (t, 1H, Ar-H), 7.332-7.374 (t, 1H, Ar-H) 7.376-7.414 (d, 1H, Ar-H), 7.415-7.443 (d, 1H, Ar-H), 7.445-7.482 (d, 1H, Ar-H), 7.485-7.542 (d, 1H,Ar-H), 7.545-7.482 (d, 1H, Ar-H), 7.641 (s, 1H, Ar-H), 7.662-7.762 (d, 1H, Ar-H), 7.764-7.789(d, 1H, Ar-H).

**EIMS (m/z) (% relative abundance):** $[M]^+$ 523.53 (100), [M+1] 524.02 (52).

Fragments: 493.07 (58), 477.10 (24), 383.08 (18), 293.05 (31), 217.02 (41), 127.98 (17), 113.96 (29).

**Elemental analysis:**

Calculated for $C_{29}H_{18}FN_3O_5S$: C, 64.56; H, 3.36; N, 7.79; Found: C, 64.52; H, 3.34; N, 7.75 %.

**(*Z*)-5-(4-fluororobenzylidene)-3-[(9*H*-carbazole-9-yl) (4-nitrophenyl) methyl] thiazolidine-2,4-dione (17e)**

**TLC analysis:** Solvent system : Benzene: Ethyl Acetate: Glacial Acetic Acid (8:1:1), $R_f$: 0.76

**Spectral data: UV $\lambda_{max}$ (DMSO):** 360.0 nm

**FTIR (KBr) (ν):** 3053.11 (Aromatic C-H str.), 1704.98 (C=O str., amide (cyclic lactums)), 1604.66 (Aromatic C=C str.), 1510.16 (Asymmetric N=O str.), 1336.58 (C-F str.), 1318.47 (Symmetric N=O str.), 1166.85 (C-N

str.), 918.12 (C-S str.), 815.83 $cm^{-1}$ (C-H def *p*-disubstituted bezene).

**$^1$H NMR (DMSO-*d*$_6$):** δ 1.625 (s, 1H, C-H), 5.397 (s, 1H, vinylic C-H), 7.104-7.132 (d, 1H, Ar-H), 7.134-7.158 (d, 1H, Ar-H), 7.161-7.183 (t, 1H, Ar-H), 7.185-7.246 (t, 1H, Ar-H), 7.247-7.272 (d, 1H, Ar-H), 7.274-7.388 (d, 1H, Ar-H) 7.390-7.508 (t, 1H, Ar-H), 7.510-7.518 (t, 1H, Ar-H) 7.521-7.558 (d, 1H, Ar-H), 7.560-7.624 (d, 1H, Ar-H), 7.625-7.642 (d, 1H, Ar-H), 7.646-7.919 (d, 1H,Ar-H), 7.921-8.021 (d, 1H, Ar-H), 8.025-8.058 (d, 1H, Ar-H), 8.061-8.202 (d, 1H, Ar-H), 8.203-8.352 ppm (d, 1H, Ar-H).

**EIMS (m/z) (% relative abundance):** $[M]^+$ 523.53(100), [M+1] 524.02 (43).

Fragments: 504.54 (38), 477.53 (29), 383.08 (23), 293.05 (22), 217.02 (36), 127.98 (22), 113.96 (34).

**Elemental analysis:**

Calculated for $C_{29}H_{18}FN_3O_4S$: C, 66.53; H, 3.47; N, 8.03; Found: C, 66.50; H, 3.45; N, 8.01 %.

**(*Z*)-5-(4-fluororobenzylidene)-3-[(9*H*-carbazole-9-yl) (4-fluorophenyl) methyl] thiazolidine-2,4-dione (17f)**

**TLC analysis:** Solvent system : Benzene: Ethyl Acetate: Glacial Acetic Acid (9.0:0.5:0.5), $R_f$: 0.67

**Spectral data: UV $\lambda_{max}$ (DMSO):** 295.0 nm

**FTIR (KBr) (ν):** 3045.47 (Aromatic C-H str.), 1703.06 (C=O str., amide (cyclic lactums)), 1593.89 (Aromatic C=C str.), 1336.58 (C-F str.), 1153.35 (C-N str.), 916.12 (C-S str.), 815.83 $cm^{-1}$ (C-H def *p*-disubstituted bezene).

**$^1$H NMR (DMSO-d$_6$)** δ 1.636 (s, 1H, C-H), 5.376 (s, 1H, vinylic C-H), 7.173-7.210 (d, 1H, Ar-H), 7.213-7.234 (d, 1H, Ar-H), 7.236-7.292 (t, 1H, Ar-H), 7.295-7.331 (t, 1H, Ar-H), 7.332-7.374 (d, 1H, Ar-H), 7.376-7.413 (d, 1H, Ar-H) 7.415-7.442 (t, 1H, Ar-H), 7.445-7.482 (t, 1H, Ar-H) 7.485-7.543 (d, 1H, Ar-H), 7.545-7.639 (d, 1H, Ar-H), 7.641-7.661 (d, 1H, Ar-H), 7.662-7.763 (d, 1H,Ar-H), 7.764-7.785 (d, 1H, Ar-H), 7.787-7.891 (d, 1H, Ar-H), 7.893-8.101 (d, 1H, Ar-H), 8.108-8.121 ppm (d, 1H, Ar-H).

**EIMS (m/z) (% relative abundance):** $[M]^+$ 496.53 (100), [M+1] 497.54 (44).

Fragments: 477.10 (22), 383.08 (19), 293.05 (25), 217.02 (26), 127.98 (17), 113.96 (24).

**Elemental analysis:**

Calculated for $C_{29}H_{18}FN_2O_2S$: C, 70.15; H, 3.65; N, 5.64; Found: C, 70.13; H, 3.63; N, 5.61 %.

**(*Z*)-5-(4-fluororobenzylidene)-3-[(9*H*-carbazole-9-yl) (3,4,5-trimethoxyphenyl) methyl] thiazolidine-2,4-dione (17g)**

**TLC analysis:** Solvent system : Benzene: Ethyl Acetate: Glacial Acetic Acid (9.0:0.5:0.5), $R_f$: 0.62

**Spectral data: UV $\lambda_{max}$ (DMSO):** 352.0 nm

**FTIR (KBr) (ν):** 3053.11 (Aromatic C-H str.), 2923.88 (Aliphatic C-H str.), 1704.08 (C=O str., amide (cyclic lactums)), 1597.09 (Aromatic C=C str.), 1338.8 (C-F str.), 1166.85 (C-N str.), 916.14 (C-S str.), 815.83 $cm^{-1}$ (C-H def *p*-disubstituted bezene).

**$^1$H NMR (DMSO-*d*$_6$)** δ 1.636 (s, 1H, C-H), 4.012 (s, 3H, $OCH_3$), 4.015 (s, 3H, $OCH_3$), 4.016 (s, 3H, $OCH_3$,) 5.376 (s, 1H, vinylic C-H), 7.213-7.234 (d, 1H, Ar-H), 7.236-7.293 (d, 1H, Ar-H), 7.295-7.331 (t, 1H, Ar-H), 7.332-7.374 (t, 1H, Ar-H), 7.376-7.412 (d, 1H, Ar-H), 7.415-7.443 (d, 1H, Ar-H) 7.445-7.484 (t, 1H, Ar-H), 7.485-7.542 (t, 1H, Ar-H) 7.545-7.639 (d, 1H, Ar-H), 7.641-7.659 (d, 1H, Ar-H), 7.662 (s, 1H, Ar-H), 7.764 (s, 1H,Ar-H), 7.787-7.891 (d, 1H, Ar-H), 7.893-7.910 ppm (d, 1H, Ar-H).

**EIMS (m/z) (% relative abundance):** $[M]^+$ 568.61(100), [M+1] 569.62 (29).

Fragments: 549.61 (51), 477.51 (39), 383.08 (23), 293.05(49), 217.02 (29), 127.98 (28), 113.96 (30).

**Elemental analysis:**

Calculated for $C_{32}H_{25}FN_2O_5S$: C, 67.59; H, 4.43; N, 4.93; Found: C, 67.56; H, 4.42; N, 4.91 %.

**(*Z*)-5-(4-fluororobenzylidene)-3-[(9*H*-carbazole-9-yl) (2-hydroxyphenyl) methyl] thiazolidine-2,4-dione (17h)**

**TLC analysis:** Solvent system: Benzene: Ethyl Acetate: Glacial Acetic Acid (9:0.5:0.5), $R_f$: 0.68

**Spectral data: UV $\lambda_{max}$ (DMSO):** 305.0 nm

**FTIR (KBr) (v):** 3417.63 (Phenolic O-H str.), 3047.32 (Aromatic C-H str.), 1704.02 (C=O str., amide (cyclic lactums)), 1593.09 (Aromatic C=C str.), 1336.58 (C-F str.), 1151.42 (C-N str.), 916.86 (C-S str.), 815.85 $cm^{-1}$ (C-H def *p*-disubstituted bezene).

**$^1$H NMR (DMSO-$d_6$):** δ 1.641 (s, 1H, C-H), 5.364 (s, 1H, vinylic C-H), 6.711 (s, 1H, phenolic O-H) 7.213-7.234 (d, 1H, Ar-H), 7.236-7.293 (t, 1H, Ar-H), 7.295-7.331 (d, 1H, Ar-H), 7.332-7.374 (t, 1H, Ar-H), 7.376-7.412 (d, 1H, Ar-H), 7.415-7.442 (d, 1H, Ar-H) 7.445-7.482 (t, 1H, Ar-H), 7.485-7.542 (t, 1H, Ar-H) 7.545-7.639 (d, 1H, Ar-H), 7.641-7.660 (d, 1H, Ar-H), 7.662-7.662 (d, 1H, Ar-H), 7.764-7.785 (d, 1H,Ar-H), 7.787-7.891 (t, 1H, Ar-H), 7.893-8.101 (d, 1H, Ar-H), 8.108-8.274 (d, 1H, Ar-H), 8.276-8.291 ppm (d, 1H, Ar-H).

**EIMS (m/z) (% relative abundance):** $[M]^+$ 494.07 (100), [M+1] 495.07 (37).

Fragments: 477.10 (44), 475.54 (32), 383.08 (24), 294.05 (29), 217.02 (38), 127.98 (17), 113.96 (28).

**Elemental analysis:**

Calculated for $C_{29}H_{18}ClFN_2O_2S$: C, 70.43; H, 3.87; N, 5.66;Found:C, 70.41; H, 3.86; N, 5.64 %.

**(*Z*)-5-(4-fluororobenzylidene)-3-[(9*H*-carbazole-9-yl) (3-hydroxyphenyl) methyl] thiazolidine-2,4-dione (17i)**

**TLC analysis:** Solvent system: Benzene: Ethyl Acetate: Glacial Acetic Acid (9.0:0.5:0.5), $R_f$: 0.64

**Spectral data: UV $\lambda_{max}$ (DMSO):** 300.0 nm

**FTIR (KBr) (v):** 3417.73 (Phenolic O-H str.) 3047.32 (Aromatic C-H str.), 1704.92 (C=O str., amide (cyclic lactums)), 1593.09 (Aromatic C=C str.), 1336.58 (C-F str.), 1151.42 (C-N str.), 919.98 (C-S str.), 815.85 (C-H def *p*-disubstituted bezene).

**$^1$H NMR (DMSO-$d_6$):** δ 1.641 (s, 1H, C-H), 5.364 (s, 1H, Vinylic C-H), 6.711 (s, 3H, Phenolic O-H) 7.213-7.234 (d, 1H, Ar-H), 7.236-7.293 (t, 1H, Ar-H), 7.295-7.331 (d, 1H, Ar-H), 7.332-7.374 (t, 1H, Ar-H), 7.376-7.412 (d, 1H, Ar-H), 7.415-7.442 (d, 1H, Ar-H) 7.445-7.483 (t, 1H, Ar-H), 7.485-7.543 (t, 1H, Ar-H) 7.545-7.539 (d, 1H, Ar-H), 7.541-7.659 (d, 1H, Ar-H), 7.662-7.762 (d, 1H, Ar-H), 7.764-7.785 (d, 1H,Ar-H), 7.787-7.892 (d, 1H, Ar-H), 7.893 (s, 1H, Ar-H), 8.108-8.274 (d, 1H, Ar-H), 8.276-8.289 ppm (d, 1H, Ar-H).

**EIMS (m/z):** $[M]^+$ 494.07(100), [M+1] 495.07 (29).

Fragments: 477.10 (52), 475.54 (34), 383.08 (27), 293.05 (26), 217.02 (42), 127.98 (23), 113.96 (34).

**Elemental analysis:** Calculated for $C_{29}H_{18}FN_2O_3S$: C, 70.43; H, 3.87; N, 5.71 Found: C, 70.42; H, 3.85; N, 5.68 %.

**(*Z*)-5-(4-fluororobenzylidene)-3-[(9*H*-carbazole-9-yl) (4-hydroxyphenyl) methyl] thiazolidine-2,4-dione (17j)**

**TLC analysis:** Solvent system : Benzene: Ethyl Acetate: Glacial Acetic Acid (9.0:0.5:0.5), $R_f$: 0.64

**Spectral data: UV $\lambda_{max}$ (DMSO):** 320.0 nm

**FTIR (KBr) (ν):** 3417.63 (Phenolic O-H str.) 3047.32 (Aromatic C-H str.), 1704.92 (C=O str., amide (cyclic lactums)), 1593.09 (Aromatic C=C str.), 1336.88 (C-F str.), 1151.42 (C-N str.), 919.98 (C-S str.), 815.83 0.5ml (C-H def *p*-disubstituted bezene).

**$^1$H NMR (DMSO-$d_6$):** δ 1.625 (s, 1H, C-H), 5.390 (s, 1H, Vinylic C-H), 7.100 (s, 3H, Phenolic O-H), 7.104-7.132 (d, 1H, Ar-H), 7.134-7.160 (d, 1H, Ar-H), 7.161-7.183 (d, 1H, Ar-H), 7.185-7.245 (d, 1H, Ar-H), 7.247-7.388 (d, 1H, Ar-H), 7.390-7.508 (d, 1H, Ar-H) 7.510-

7.520 (t, 1H, Ar-H), 7.521-7.558 (t, 1H, Ar-H) 7.560-7.623 (d, 1H, Ar-H), 7.625-7.644 (d, 1H, Ar-H), 7.646-7.918 (d, 1H, Ar-H), 7.921-8.023 (d, 1H,Ar-H), 8.025-7.060 (d, 1H, Ar-H), 8.061-8.223 (d, 1H, Ar-H), 8.225-8.274 (d, 1H, Ar-H), 8.276-8.289 ppm (d, 1H, Ar-H).

**EIMS (m/z) (% relative abundance):** $[M]^+$ 494.07 (100), [M+1] 495.07 (32).

Fragments: 477.10 (49), 475.54 (38), 383.08 (21), 294.05 (29), 217.02 (42), 127.98 (14), 113.96 (24).

**Elemental analysis:**

Calculated for $C_{29}H_{18}FN_2O_3S$: C, 70.43; H, 3.87; N, 5.66; Found: C, 70.41; H, 3.85; N, 5.63 %.

**Pharmacology**

**Antibacterial activity**

The antibacterial activity of newly synthesized compounds was tested by paper disc diffusion method using nutrient agar medium against following microorganism: ***Staphyllococcus aureus, Bacillus subtilis,*** (Gram positive) and ***Escherichia coli, Pseudomonas aeureginosa*** (Gram negative).

In the paper disc-diffusion method, paper disc impregnated with compounds dissolved in DMSO at concentration 25, 50 and 100 μg $ml^{-1}$ were used. Disc impregnated with DMSO were used as solvent control for antibacterial activity because of free solubility of test compounds. The microorganism culture was spread over nutrient agar media in Petri dishes, and then the disc impregnated with the solution was placed on the surface of the media inoculated with the bacterial strain.

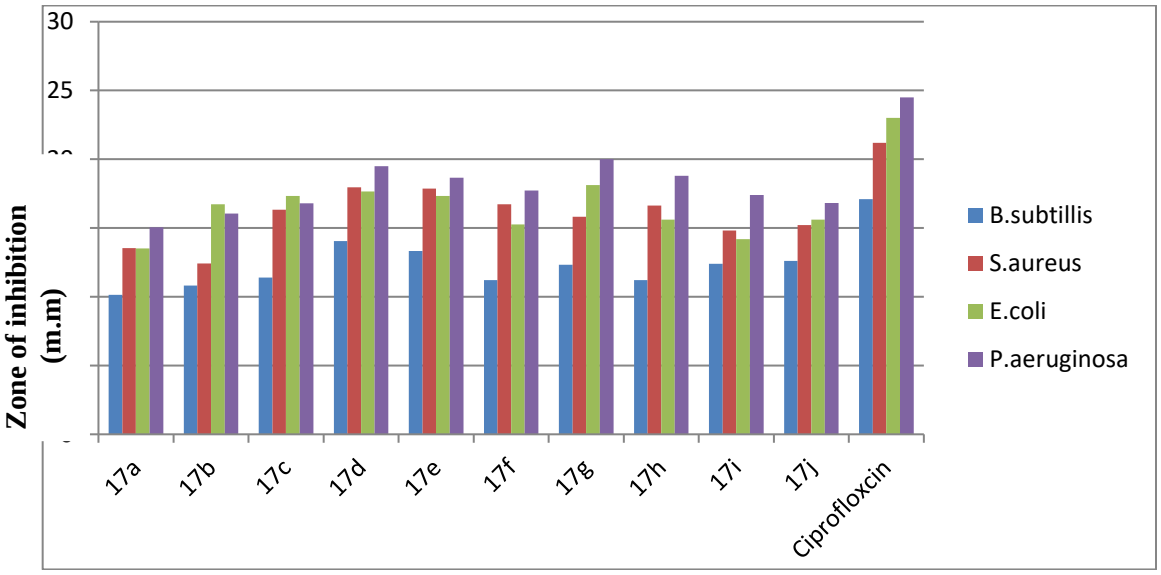
The plates were incubated at 35°C for 24 hrs for bacterial cultures. After incubation, the zones of inhibition around the disc were observed. The zones of inhibition indicate that the compounds inhibit growth of microorganism. Each testing is done in triplicate. Ciprofloxacin at conc. 50μg $ml^{-1}$ was used as standard drug for antibacterial activity. Results were interpreted in terms of diameter (mm) of zone of inhibition.

**Table 1: Antibacterial activity of synthesized compounds for gram positive strains**

| **Code of Compounds** | **Diameter of zone of inhibition in mm [mean ± S.D. (n=3)]** | | | | | |
|---|---|---|---|---|---|---|
| | ***B.subtilis*** | | | ***S.aureus*** | | |
| | **25 μg $ml^{-1}$** | **50 μg $ml^{-1}$** | **100 μg $ml^{-1}$** | **25 μg $ml^{-1}$** | **50 μg $ml^{-1}$** | **100 μg $ml^{-1}$** |
| **17a** | 7.51 ± 0.31 | 10.13 ± 0.70 | 13.41 ± 0.80 | 7.21 ± 0.40 | 13.53 ± 1.13 | 17.26 ± 0.75 |
| **17b** | 7.43 ± 0.30 | 10.81 ± 0.60 | 13.40 ± 0.52 | 6.53 ± 0.33 | 12.42 ± 0.52 | 14.12 ± 0.23 |
| **17c** | 7.26 ± 0.32 | 11.40 ± 0.52 | 15.93 ± 0.30 | 8.62 ± 0.52 | 16.33 ± 0.46 | 18.12 ± 0.52 |
| **17d** | 8.86 ± 0.30 | 14.06 ± 0.64 | 17.96 ± 0.41 | 9.83 ± 0.11 | 17.96 ± 0.32 | 19.96 ± 0.11 |
| **17e** | 8.13 ± 0.11 | 13.33 ± 0.31 | 17.40 ± 0.22 | 9.66 ± 0.11 | 17.86 ± 0.11 | 19.80 ± 0.26 |
| **17f** | 7.73 ± 0.11 | 11.20 ± 0.52 | 16.66 ± 0.33 | 7.53 ± 0.31 | 16.73 ± 0.61 | 19.66 ± 0.30 |
| **17g** | 7.26 ± 0.31 | 12.33 ± 0.11 | 16.60 ± 0.21 | 8.26 ± 0.33 | 15.81 ± 0.41 | 18.23 ± 0.24 |
| **17h** | 6.46 ± 0.51 | 11.21 ± 0.22 | 17.10 ± 0.20 | 8.13 ± 0.30 | 16.63 ± 0.20 | 17.86 ± 0.61 |
| **17i** | 6.20 ± 0.42 | 12.40 ± 0.31 | 14.12 ± 0.43 | 7.80 ± 0.12 | 14.82 ± 0.42 | 18.60 ± 0.34 |
| **17j** | 7.41 ± 0.51 | 12.61 ± 0.22 | 13.80 ± 0.24 | 8.82 ± 0.34 | 15.21 ± 0.11 | 19.81 ± 0.52 |
| **Ciprofloxacin** | - | 17.10 ± 0.20 | - | - | 21.20 ± 0.80 | - |

**Table 2: Antibacterial activity of synthesized compounds for gram negative strains**

| Code of Compounds | Diameter of zone of inhibition in mm [mean ± S.D. (n=3)] | | | | | |
|---|---|---|---|---|---|---|
| | *E.coli* | | | *P.aeruginosa* | | |
| | 25 µg $ml^{-1}$ | 50 µg $ml^{-1}$ | 100 µg $ml^{-1}$ | 25 µg $ml^{-1}$ | 50 µg $ml^{-1}$ | 100 µg $ml^{-1}$ |
| **17a** | 9.26 ± 0.75 | 13.51 ± 0.13 | 17.26 ± 0.75 | 9.81 ± 0.60 | 15.06 ± 0.75 | 18.26 ± 0.50 |
| **17b** | 8.46 ± 0.41 | 16.73 ± 0.10 | 18.90 ± .26 | 10.16 ± 0.30 | 16.06 ± 0.80 | 20.2 0± 0.87 |
| **17c** | 9.22 ± 0.52 | 17.33 ± 0.30 | 18.26 ± 0.41 | 10.13 ± 0.32 | 16.80 ± 0.42 | 20.46 ± 0.70 |
| **17d** | 10.53 ± 0.32 | 17.66 ± 0.61 | 19.96 ± 0.50 | 10.23 ± 0.21 | 19.50 ± 0.60 | 21.66 ± 0.41 |
| **17e** | 10.25 ± 0.23 | 17.32 ± 0.41 | 19.82 ± 0.21 | 10.42 ± 0.22 | 18.65 ± 0.52 | 21.33 ± 0.30 |
| **17f** | 9.44 ± 0.21 | 15.26 ± 0.41 | 17.53 ± 0.71 | 9.93 ± 0.41 | 17.73 ± 0.11 | 19.06 ± 0.41 |
| **17g** | 10.93 ± 0.11 | 18.13 ± 0.52 | 22.81 ± 0.62 | 10.86 ± 0.50 | 20.0 ± 0.30 | 22.42± 0.52 |
| **17h** | 9.64 ± 0.52 | 15.60 ± 0.91 | 18.20 ± 0.60 | 9.73 ± 0.51 | 18.80 ± 0.61 | 18.46 ± 0.41 |
| **17i** | 9.22 ± 0.20 | 14.20 ± 0.82 | 19.10 ± 0.63 | 10.81 ± 0.21 | 17.40 ± 0.30 | 20.8 0± 0.42 |
| **17j** | 9.12 ± 0.31 | 15.60 ± 0.33 | 20.25 ± 0.01 | 8.60 ± 0.12 | 16.81 ± 0.20 | 19.70 ± 0.23 |
| **Ciprofloxacin** | - | 23.00 ± 0.56 | - | - | 24.50 ± 0.75 | - |




**Graph 1 : Showing antibacterial activity of synthesized compounds [17a-j] and ciprofloxacin as a standard drug at 50µg/ml concentration.**

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