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One Pot Synthesis of Potentially Biologically Active Novel 4-Thiazolidinone Derivatives

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Novel compounds of series **1a-j** and **2a-j** were synthesized by adopting environment friendly methodology, with an idea that these compounds are tested for their antibacterial activity. In combination to microwave radiation with montmorillonite clays (K10 and KSF types) were used as solid phase catalysts. The catalytic efficiency of montmorillonite KSF was marginally inferior to that of montmorillonite K10. The average yield of all compounds of (**1a-j**) was found 88.3 and 88.5 % for the compounds (**2a-j**). Structural elucidation was carried out using FTIR, ^{1}H NMR, elemental analyzer and MS. The synthesized compounds were checked for their antibacterial activity (*in vivo*) and found that the compounds **1g**, **1h**, **2g** and **2j** exhibited comparable or higher antibacterial activity then reference standard against *E. coli*, *S. enteritidis*, *P. aeruginosa*, *S. aureus* and *B. subtilis*. Most of the compounds of series-2 showed significant activity as compared with ciprofloxacin. These compounds could be lead to the selection and use as efficient antimicrobial agents, especially for the treatment of multi-drug resistant infections.

Key Words: Microwave irradiation, Montmorillonite, 4-Thiazolidinone.

INTRODUCTION

4-Thiazolidinone is an important precursor known to be associated with several biological activates[1,2]. These observations served as an impetus for the extension of investigation in the field of synthesis of 4-thiazolidione derivatives in the hope of discovering compounds with good pharmacological properties. Bacteria are developing resistance against existing antibiotics. There is always need to develop new antibiotics. Thiazolidinone derivatives are known to possess diversified antibacterial, antifungal and antiviral properties. For this reason, a variety of 4-thiazolidinone based compounds and intermediates have been prepared in this study and these compounds were tested for diverse biological activities.

In order to reduce the environmental impact there is a need for clean chemical processes including monitoring analysis, synthetic procedures, catalysts and reaction conditions[3]. To achieve these goals, green chemistry is being developed based on innovative and unconventional synthetic procedures including reactions carried out in water[4,5] (normal[6] and super heated under high pressure[7]), in supercritical fluids[8,9], in ionic liquids[10], in micro emulsions[11], in solvent free conditions[12], by ultrasounds[13] and microwaves[14,15] that must allow products to be prepared with high yields.

Microwave irradiation (non-conventional methods) takes a particular place as it induces specific interaction between materials and wave of electromagnetic nature assimilated to dielectric heating[16,17]. Heating by microwaves is therefore an original procedure to bring the advantages of speed, no inertia, quick energy transfer and no superficial over heating. Microwaves can be used to promote many organic synthesis; the material-wave interactions produce uniform heating of the reaction medium.

EXPERIMENTAL

Melting points were measured on a digital melting point apparatus and IR spectra were recorded on a Bruker Tensor 27 FT-IR Spectrometer. ^{1}H and ^{13}C NMR spectra were recorded Bruker AVANCE 300 (300.13 MHz for ^{1}H and 75.5 MHz for ^{13}C NMR) and TMS was used as internal standard. The instrument Bruker Esquire 3000 + ion trap with ESI ionization was used for mass spectrometric analysis. Elemental analysis of carbon, hydrogen, nitrogen and sulfur were carried out on 2400-CHN analyzer (Perkin Elmer) and 932 Leco CHNS analyzer (Leco). All chemicals were purchased from Merck, Fluka, Sigma-Aldrich and used as such without purification. TLC coated with silica 60 F_{254} aluminum plates were purchased from Merck (Germany).

Microwave: Microwave irradiations were carried out in a SINEO (MAS-II) microwave system with dynamically adjustable microwave power 0-1000W into ten ranges, increment

100 W based on reaction temperature. Calibrated digital dual channel temperature monitor ranging from ambient to 400 ºC was used. In this advance microwave system ten reaction methods can be programmed in which four reaction variables are changeable in each *e.g.*, time, temperature, stirring speed and microwave power. Reaction processes were observed with on site camera.

Microwave procedure-I: multi-component reaction using montmorillonite clays (K-10 and KSF)

2-(2,5-Dimethylphenyl)-3-(4-methoxypyrimidin-2-yl)-thiazolidin-4-one (1a): A mixture of 4-methoxypyrimidin-2-amine (5 mmol, 0.625 g), 2,5-dimethylbenzaldehyde (5 mmol; 0.670 g), thioglycolic acid (5 mmol; 0.460 g) and montmorillonite clay (K-10 and KSF; 30 % by weight of total of reactants) was taken in a round bottom flask equipped with a reflux condenser. The reaction mixture was stirred and irradiated in microwave oven at 200 watt for 8 min at 105-110 ºC. The reaction was monitored by TLC and the mixture was cooled to room temperature, added ethyl acetate (25 mL), the mixture was neutralized with a solution of sodium hydrogen carbonate. The solvent was removed under reduced pressure to get a crude product (oily residue). The crude product was purified with silica gel flash chromatography eluting with chloroform and recrystalized from ethanol.

Microwave procedure-II: Solvent free, multi-component reaction (1a): A mixture of 4-methoxypyrimidin-2-amine (5 mmol; 0.625 g), 2,5-dimethylbenzaldehyde (5 mmol; 0.670 g), thioglycolic acid (5 mmol; 0.460 g) was taken in a round bottom flask equipped with a reflux condenser. The reaction mixture was irradiated in microwave oven at 200 watt for 8 min at 105-110 ºC. The mixture was cooled to room tempe-rature and recrystallized from ethanol.

Series-2 (2a-j)

Microwave procedure-I: Multi-component reaction using montmorillonite clays (K-10 and KSF)

5-Benzylidene-3-phenyl-2-thioxo-thiazolidin-4-one (2a): A mixture of phenyl amine (0.465 g, 5 mmol), benzaldehyde (0.53 g, 5 mmol), sulfanyl(thioxo)acetic acid (0.55 g, 5 mmol) and montmorillonite clays, KSF and K-10 (30 % by weight of reactants) was irradiated under microwave radiation (200 watt) at 110 ºC temperature for 12 min. The final product was cooled to 25 ºC, washed with water, dried under suction and recrystallized from DMF: H_2O (5:5 by v/v) to obtain the compound 5-benzylidene-3-phenyl-2-thioxothiazolidin-4-one (**2a**) (yields 87.6 % with K-10 and 78.4 % with KSF).

Microwave procedure-II: solvent free, multi-component reaction: A mixture of substituted aromatic amines, substituted benzaldehydes, sulfanyl(thioxo)acetic acid and irradiated under microwave radiation (200 watt) at 110 ºC for 12 min. The reaction was monitored by TLC and the product was cooled to room temperature. The crude product washed with water, dried under suction and recrystallized from DMF: H_2O (5:5 by v/v) to get compounds (**2a-j**) (ranged from 34-79 %).

Methodology for antibacterial screening: Mueller-Hinton agar (MHA) medium[18] was prepared by dissolving agar in 250 mL distilled water with slow heating and stirring to dissolve the medium completely. It was sterilized in autoclave at 15 PSI pressure and 121 ºC temperature for 15 min. The sterilized medium was immediately poured into petri dishes to form a uniform layer (2-5 mm thick). The petri dishes were stored in incubator so that no appreciable growth of the microorganisms was observed before the dishes were used[19]. Solutions of synthesized compounds (50 mg/mL) and reference substances were prepared that were presumed to be of equal concentration. The solutions of 10 µL of synthesized compound and reference standard were applied to the surface of the medium (6 mm in diameter) in triplicate, in cavities prepared in the agar. Negative controls were prepared by using N,N-dimethylformamide (DMF) which was employed to dissolve the test compounds. The inoculated plates were incubated at 37 ºC for 24-48 h[20]. Antibacterial activities of synthesized compounds were calculated quantitatively (bio assay) by measuring the zone of inhibition (mm) against test organisms of synthesized compounds and compared with the zone of inhibition of reference standards (measured the diameters with a precision of at 0.1 mm). All bacterial strains were cultured on their respective medium for further bacterial propagation[21].

2-(2,5-Dimethylphenyl)-3-(4-methoxypyrimidin-2-yl)-4-thiazolidinone (1a): Yield 92 %, m.p. 186-188 ºC; IR (KBr, ν_{max}, cm^{-1}): 3340, 3266, 3007, 2934, 1720 (C=O), 1591, 1181. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 2.35 (s, 6H, $2CH_3$), 3.38 (d, 2H, $C_{5\text{-thiazolidinoe}}$ J = 13.7Hz), 3.73 (s, 3H, OCH_3), 5.92 ($C_{2\text{-thiazolidinoe}}$), 6.82-6.75 (m, 3H), 8.90 (s, 1H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 17.4 (CH_3), 24.6, 33.6 ($C_{5\text{-thiazolidinoe}}$), 55.9 ($OCH_3$), 59.4($C_{2\text{-thiazolidinoe}}$), 105.1, 127.4, 128.9, 130.5, 133.6, 135.3, 138.9, 157.0, 158.5, 1170.6 (C-O-CH_3), 171.2 (C=O). MS m/z: 315.10 (M + 1, 100 %); anal.: $C_{16}H_{17}N_3O_2S$: (315.39): Calcd. (%): C, 60.93; H, 5.43; N, 13.32; O, 10.15, S, 10.17, Found (%): C, 60.96; H, 5.42; N, 13.35; O, 10.10, S, 10.18.

2-(4-Ethylphenyl)-3-(4-methoxypyrimidin-2-yl)-4-thiazolidinone (1b): Yield 91 %, m.p. 223-225 ºC; IR (KBr, ν_{max}, cm^{-1}): 3340, 3266, 3007, 2934, 1720 (C=O), 1591, 1181. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.24 (s, 3H, CH3), 2.59 (s, 2H, CH_2), 3.29 (d, 1H, J = 13.6 Hz), 3.40 (d, 1H, J = 13.7 Hz), 3.73 (s, 3H, OCH_3), 5.90 ($C_{2\text{-thiazolidinoe}}$), 6.70 (s, 1H), 7.09-6.88 (m, 4H), 8.56 (s, 1H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 14.6 (CH_3), 32.7, 33.6 ($C_{5\text{-thiazolidinoe}}$), 55.9 ($OCH_3$), 65.9 ($C_{2\text{-thiazolidinoe}}$), 105.1, 126.0, 126.2, 128.6, 129.3, 139.1, 139.4, 157.0, 158.5, 170.6 (C-O-CH_3), 171.2 (C=O). MS m/z (%): 315.10 (100.0 %); anal. (%): $C_{16}H_{17}N_3O_2S$: 315.39 calcd. (%): C, 60.93; H, 5.43; N, 13.32; O, 10.15, S, 10.17. Found (%): C, 60.90; H, 5.45; N, 13.30; O, 10.18, S, 10.12.

2-(4-Methoxyphenyl)-3-(4-methoxypyrimidin-2-yl)-thiazolidin-4-one (1c): Yield 89 %, m.p. 202-204 ºC; IR (KBr, ν_{max}, cm^{-1}): 3340, 3266, 3007, 2934, 1720 (C=O), 1591, 1181: ^{1}H NMR (300 MHz, $CDCl_3$) δ: 3.38(d, 2H, J = 6.6 Hz, $C_{5\text{-thiazolidinoe}}$), 3.73 (s, 6H, $2OCH_3$), 5.92 ($C_{2\text{-thiazolidinoe}}$), 6.70 (s, 1H), 7.03-6.57 (m, 4H), 8.54 (s, 1H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 33.6 ($C_{5\text{-thiazolidinoe}}$), 55.9 ($OCH_3$), 65.9 ($C_{2\text{-thiazolidinoe}}$), 105.1, 112.7, 112.8, 121.1, 129.7, 157.0, 158.5, 160.6 (C-O-CH_3), 170.6 (C-O-CH_3), 171.2 (C=O). MS m/z (%): 317.08 (M + 1140.2, 100 %). Anal. (%): $C_{15}H_{15}N_3O_3S$; 317.36: Calcd. (%): C, 56.77; H, 4.76, N, 13.24; O, 15.12; S, 10.10, Found (%): C, 56.78; H, 4.75, N, 13.28; O, 15.10; S, 10.08.

2-(2-Hydroxy-5-methoxyphenyl)-3-(4-methoxypyrimidin-2-yl)-thiazolidin-4-one (1d): Yield 94 %, m.p. 212-214 ºC; IR (KBr, ν_{max}, cm^{-1}) 3340, 3266, 3007, 2934, 1720 (C=O), 1591, 1181. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 3.38 (d, 2H, *J* = 6.7 Hz, $C_{5\text{-thiazolidinoe}}$), 3.73 (s, 6H, $2OCH_3$), 5.0 (s, 1H, OH), 5.92 ($C_{2\text{-thiazolidinoe}}$), 6.50-6.41 (m, 3H), 8.55 (s, 1H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 33.6 ($C_{5\text{-thiazolidinoe}}$), 55.7 ($C_{2\text{-thiazolidinoe}}$), 55.9 ($OCH_3$), 105.1, 114.1, 114.2, 116.8, 119.2, 148.2, 153.2 (C-O-CH_3), 157.0, 158.5, 170.6 (C-O-CH_3), 171.2 (C=O). MS m/z (%): 333.08 (M + 1, 100 %). Anal.: $C_{15}H_{15}N_3O_4S$: 333.36: Calcd. (%): C, 54.04; H, 4.54; N, 12.60; O, 19.20; S, 9.62. Found (%): C, 54.02; H, 4.55; N, 12.56; O, 19.22; S, 9.60.

2-(4-Ethoxyphenyl)-3-(4-methoxypyrimidin-2-yl)-thiazolidin-4-one (1e): Yield 87 %, m.p. 214-216 ºC; IR (KBr, ν_{max}, cm^{-1}): 3340, 3266, 3007, 2934, 1720 (C=O), 1591, 1181. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.33 (s, 3H, OCH_2CH_3), 3.38 (d, 2H, *J* = 6.7Hz, $C_{5\text{-thiazolidinoe}}$), 3.73 (s, 3H, OCH_3), 3.98 (d, 2H, OCH_2CH_3), 5.92 (s, 1H, $C_{2\text{-thiazolidinoe}}$), 6.62-6.57 (m, 4H), 6.78 (s, 1H), 8.55 (s, 1H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 14.8, 33.6 ($C_{5\text{-thiazolidinoe}}$), 55.9 ($OCH_3$), 64.7, 65.9 ($C_{2\text{-thiazolidinoe}}$), 105.1, 112.8, 112.9, 120.4, 129.3, 139.8, 157.0, 157.4 (C-$CHOCH_3$), 170.6 (C-O-CH_3), 158.5, 171.2 (C=O). MS m/z (%): 331.1 (M + 1, 100 %) Anal.: $C_{16}H_{17}N_3O_3S$: 331.39: Calcd. (%): C, 57.99; H, 5.17; N, 12.68; O, 14.48; S, 9.68. Found (%): C, 57.97; H, 5.15; N, 12.70; O, 14.46; S, 9.64.

2-[4-(Dimethylamino)phenyl]-3-(4-methoxypyrimidin-2-yl)-4-thiazolidinone (1f): Yield 79 %, m.p. 224-226 ºC, IR (KBr, ν_{max}, cm^{-1}): 3340, 3266, 3007, 2934, 1714, 1591, 1181. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.00(s, 1H), 7.24 (d, 2H, *J* = 6.3 Hz), 7.48 (CH=$C_{5\text{-thiazolidinoe}}$), 7.54 (d, 2H, *J* = 5.6 Hz), 7.64 (d, 2H, *J* = 7.2 Hz), 8.14 (d, 2H, *J* = 7.7 Hz). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 120.0, 120.4, 123.5, 124.1, 127.1, 128.7, 138.2, 141.0, (CH=$C_{5\text{-thiazolidinoe}}$), 142.0, 147.6, 163.8 (C=O), 193.0 (C=S). MS m/z: 331.12 (M + 1, 100 %) Anal.: $C_{16}H_{10}N_2O_3S_2$: (330.40): Calcd. (%): C, 58.16; H, 5.49; N, 16.96; O, 9.68; S, 9.70; found (%): C, 58.14; H, 5.47; N, 16.94; O, 9.65; S, 9.68.

2-(2,5-Dichlorophenyl)-3-(4-methoxypyrimidin-2-yl)-thiazolidin-4-one (1g): Yield: 87 %, m.p. 226-228 ºC; IR (KBr, ν_{max}, cm^{-1}): 3340, 3266, 3007, 2934, 1714, 1591, 1181. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 3.38 (d, 2H, *J* = 6.7 Hz, $C_{5\text{-thiazolidinoe}}$). 3.73 (s, 3H, OCH_3), 5.92 (s, 1H, $C_{2\text{-thiazolidinoe}}$), 7.09-7.01 (m, 3H), 6.70 (s, 1H), 8.55 (s, 1H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 33.6 ($C_{5\text{-thiazolidinoe}}$), 55.9 ($OCH_3$), 56.0 ($C_{2\text{-thiazolidinoe}}$), 104.0, 105.1, 128.7, 130.0, 130.2, 132.3, 157.0, 158.5, 170.6 (C-O-CH_3), 171.2 (C=O). MS m/z: 354.99 (M + 1, 100 %) Anal.: $C_{14}H_{11}Cl_2N_3O_2S$: 356.23: Calcd. (%): C, 47.20; H, 3.11; N, 11.80; O, 8.98; S, 9.00. Found (%): C, 47.18; H, 3.12; N, 11.78; O, 8.96; S, 9.02.

2-(2,5-Difluorophenyl)-3-(4-methoxypyrimidin-2-yl)-thiazolidin-4-one (1h): Yield 88 % m.p. 221-223 ºC; IR (KBr, ν_{max}, cm^{-1}): 3340, 3266, 3007, 2934, 1714, 1591, 1181. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 3.38 (d, 2H, *J* = 6.7 Hz, $C_{5\text{-thiazolidinoe}}$), 3.73 (s, 3H, OCH_3), 5.92 (s, 1H, $C_{2\text{-thiazolidinoe}}$), 6.83-6.75 (m, 3H), 6.70 (s, 1H), 8.55 (s, 1H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 33.6 ($C_{5\text{-thiazolidinoe}}$), 54.8 ($C_{2\text{-thiazolidinoe}}$), 55.9 ($OCH_3$), 105.1, 103.5, 115.5, 117.0, 117.4, 157.0, 158.4 (C-F), 158.5, 166.9 (C-F), 170.6 (C-O-CH_3), 171.2 (C=O). MS m/z: 323.05 (M + 1, 100 %). Anal.: $C_{14}H_{11}F_2N_3O_2S$: 323.32: Calcd. (%): C, 52.01; H, 3.43; N, 13.00; O, 9.90; S, 9.92, Found (%): C, 52.03; H, 3.45; N, 13.02; O, 9.92; S, 9.94.

2-(2,5-Dihydroxyphenyl)-3-(4-methoxypyrimidin-2-yl)-thiazolidin-4-one (1i): Yield 94 % m.p. 206-208 ºC; IR (KBr, ν_{max}, cm^{-1}): 3340, 3266, 3007, 2934, 1714, 1591, 1181. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 3.38 (d, 2H, *J* = 6.7 Hz, $C_{5\text{-thiazolidinoe}}$), 3.73 (s, 3H, OCH_3), 5.0 (s, 2H, OH), 5.92 (s, 1H, $C_{2\text{-thiazolidinoe}}$), 6.44-6.36 (m, 3H), 6.70 (s, 1H), 8.55 (s, 1H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 33.6 ($C_{5\text{-thiazolidinoe}}$), 55.7 ($C_{2\text{-thiazolidinoe}}$), 55.9 ($OCH_3$), 105.1, 115.7, 115.8, 117.2, 119.6, 148.5, 151.0, 157.0, 158.5, 170.6 (C-O-CH_3), 171.2 (C=O). MS m/z: 319.06 (M + 1, 100 %), Anal.: $C_{14}H_{13}N_3O_4S$: 319.34: Calcd. (%): C, 52.66; H, 4.10; N, 13.16, O, 20.04; S, 10.04, Found (%): C, 52.68; H, 4.12; N, 13.14, O, 20.02; S, 10.01.

2-[3-(Furan-2-yl)phenyl]-3-(4-methoxypyrimidin-2-yl)-thiazolidin-4-one (1j): Yield 83 %, m.p. 198-200 ºC; IR (KBr, ν_{max}, cm^{-1}): 3340, 3266, 3007, 2934, 1714, 1591, 1181. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 3.38 (d, 2H, *J* = 6.6 Hz, $C_{5\text{-thiazolidinoe}}$) 3.73 (s, 3H, OCH_3), 5.92 (s, 1H, $C_{2\text{-thiazolidinoe}}$), 6.3 (d, 2H, *J* = 7.4 Hz), 6.70 (s, 1H), 7.28-7.02 (m, 3H), 7.40 (s, 1H), 8.55 (s, 1H). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 33.6 ($C_{5\text{-thiazolidinoe}}$), 55.9 ($OCH_3$), 65.3 ($C_{2\text{-thiazolidinoe}}$), 105.0, 105.1, 107.2, 125.9, 128.7, 129.2, 130.1, 130.3, 139.7, 142.9, 154.0, 157.0, 158.5, 170.6 (C-O-CH_3), 171.2 (C=O). MS m/z: 353.08 (M + 1, 100 %). Anal.: $C_{18}H_{15}N_3O_3S$: 353.40: Calcd. (%): C, 61.18; H, 4.28: N, 11.89; O, 13.58; S, 9.07. Found (%): C, 61.16; H, 4.26: N, 11.87; O, 13.54, S, 9.03.

5-Benzylidene-3-phenyl-2-thioxo-thiazolidin-4-one (2a): Yield 87.6 %, m.p. 223-225 ºC; IR (KBr, ν_{max}, cm^{-1}): 3266, 3020, 2934, 1714. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 6.80 (s, 1H, CH=$C_{5\text{-thiazolidinoe}}$), 7.04 (s, 1H), 7.14 (s, 1H), 7.21 (d, 2H, *J* = 5.3 Hz), 7.24 (d, 2H, *J* = 5.7 Hz), 7.30 (d, 2H, *J* = 6.6 Hz), 7.58-7.04 (10 H, aromatic protons), 7.62 (d, 2H, *J* = 7.7 Hz). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 120.0, 120.4, 124.1, 126.2, 127.7, 128.4, 128.7, 134.9, 138.2, 193.0 (C=S), 142.0 (CH=$C_{5\text{-thiazolidinoe}}$), 163.8 (C=O). MS m/z: 297.03 (M + 1) 219, 206, 143, 90, 77. Anal.: $C_{16}H_{11}NOS_2$: (297.39): Calcd. (%): C, 64.62; H, 3.73; N, 4.71; O, 5.38; S, 21.56. Found (%): C, 64.68; H, 3.67; N, 4.66; O, 5.32; S, 21.53.

5-(4-Methylbenzylidene)-3-phenyl-2-thioxo-thiazolidin-4-one (2b): Yield 89 %, m.p. 223-225 ºC; IR (KBr, ν_{max}, cm^{-1}): 3265, 3018, 2914, 1716. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.60-7.04 (9 H, aromatic protons), 7.60 (d, 2H, *J* = 7.6 Hz), 7.24 (d, 2H, *J* = 6.7 Hz), 7.18 (d, 2H, *J* = 5.8 Hz), 7.10 (d, 2H, *J* = 6.5 Hz), 7.04 (s, 1H), 6.76 (CH=$C_{5\text{-thiazolidinone}}$), 2.35 (s, 3H, CH_3). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 193.0 (C=S), 163.8 (C=O), 142.0 (CH=$C_{5\text{-thiazolidinone}}$), 138.2, 136.9, 131.9, 129.1, 128.7, 126.1, 124.1, 120.4, 120.0, 20.9. MS m/z: 311.04 (M + 1), 219, 129, 104, 84. Anal.: $C_{17}H_{13}NOS_2$: (311.42); calcd. (%): C, 65.56; H, 4.21; N, 4.50; O, 5.14; S, 20.59. Found (%): C, 65.48; H, 4.16; N, 4.42; O, 5.11; S, 20.56.

5-(4-Methoxybenzylidene)-3-phenyl-2-thioxo-thiazolidin-4-one (2c): Yield 90 %, m.p. 202-204 ºC; IR (KBr, ν_{max}, cm^{-1}): 3278, 3034, 2944, 1719. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 3.73 (s, 3H, OCH_3), 6.74 (CH=$C_{5\text{-thiazolidinoe}}$), 7.04 (d, 2H, *J* = 6.0 Hz)], 7.12 (s, 1H),7.16 (d, 2H, *J* = 6.8 Hz), 7.26

(d, 2H, *J* = 6.6 Hz),7.62-7.04 (9 H, aromatic protons), 7.68 (d, 2H, *J* = 7.5 Hz). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 56.3 (OCH_3) 114.4, 115.4, 119.8, 120.0, 120.4, 124.1, 128.6, 128.7, 129.8, 138.2, 148.4, 142.0 (CH=$C_{5\text{-thiazolidinone}}$), 163.8 (C=O), 193.0 (C=S). MS m/z: 327.04 (M + 1), 220, 143, 120, 77. Anal.: $C_{17}H_{13}NO_2S_2$: (327.42): calcd. (%): C, 62.36; H, 4.00; N, 4.28; O, 9.77; S, 19.59. Found (%): C, 62.32; H, 4.06; N, 4.25; O, 9.76; S, 19.54.

5-(3-Hydroxy-4-methoxybenzylidene)-3-phenyl-2-thioxo-thiazolidin-4-one (2d): Yield 92 %, m.p. 198-200 ºC; IR (KBr, ν_{max}, cm^{-1}): 3348, 3260, 3023, 2929, 1720. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 3.73 (s, 3H, OCH_3), 5.0 (s, 1H, OH), 6.72 (CH=$C_{5\text{-thiazolidinone}}$), 7.02 (d, 2H, *J* = 6.0 Hz), 7.12 (s, 1H), 7.16 (d, 2H, *J* = 6.8 Hz), 7.24 (d, 2H, *J* = 7.00 Hz), 7.02-7.64 (9 H, aromatic protons), 7.69 (d, 2H, *J* = 7.8 Hz). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 56.3 (OCH_3), 114.4, 115.4, 119.8, 120.0, 120.4, 124.1, 128.6, 128.7, 138.2, 142.0 (CH=$C_{5\text{-thiazolidinone}}$), 142.8, 148.4, 163.8 (C=O), 193.0 (C=S). MS m/z: 343.03 (M + 1), 219, 136, 77. Anal.: $C_{17}H_{13}NO_3S_2$: (343.42): Calcd. (%): C, 59.46; H, 3.82; N, 4.08; O, 13.98; S, 18.67; found (%): C, 59.48; H, 3.88; N, 4.12; O, 13.90; S, 18.65.

5-[4-(Dimethylamino)benzylidene]-3-phenyl-2-thioxo-thiazolidin-4-one (2e): Yield 94 %, m.p. 210-212 ºC; IR (KBr, ν_{max}, cm^{-1}): 3220, 3012, 2932, 1714. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.64-6.98 (9 H, aromatic protons), 7.64 (d, 2H, *J* = 7.8Hz), 7.28 (d, 2H, *J* = 7.00 Hz), 7.18 (d, 2H, *J* = 6.8 Hz), 7.12 (s, 1H), 6.98 (d, 2H, *J* = 6.0 Hz)], 6.78 (CH=$C_{5\text{-thiazolidinone}}$), 2.85 (s, 6H, $N(CH_3)_2$). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 193.0 (C=S), 163.8 (C=O), 143.7, 142.0, (CH=$C_{5\text{-thiazolidinone}}$), 138.2, 128.7, 127.1, 124.4, 124.1, 120.4, 120.0, 113.0, 43.6 ($N(CH_3)_2$). MS m/z: 340.07 (M + 1), 219, 143, 133, 77. Anal.: $C_{18}H_{16}N_2OS_2$: (340.46): calcd. (%): C, 63.50; H, 4.74; N, 8.23; O, 4.70; S, 18.84. Found (%): C, 63.56; H, 4.78; N, 8.27; O, 4.76; S, 18.80.

5-(4-Nitrobenzylidene)-3-phenyl-2-thioxo-thiazolidin-4-one (2f): Yield 79 %, m.p. 224-226 ºC; IR (KBr, ν_{max}, cm^{-1}): 3264, 3030, 2934, 1718. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 6.78 (CH=$C_{5\text{-thiazolidinone}}$), 7.18 (s, 1H), 7.26 (d, 2H, *J* = 6.3 Hz), 7.52 (d, 2H, *J* = 6.5 Hz), 7.64 (d, 2H, *J* = 6.30 Hz), 7.98-7.18 (9 H, aromatic protons), 8.24 (d, 2H, *J* = 5.7 Hz). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 120.0, 120.4, 123.5, 124.1, 127.1, 128.7, 138.2, 141.0, 142.0 (CH=$C_{5\text{-thiazolidinone}}$), 147.6, 163.8 (C=O), 193.0 (C=S). MS m/z: 342.01 (M + 1), 219, 143, 135, 77; Anal.: $C_{16}H_{10}N_2O_3S_2$: (342.39); calcd. (%): C, 56.13; H, 2.94; N, 8.18; O, 14.02; S, 18.73; found (%): C, 56.09; H, 2.98; N, 8.12; O, 14.06; S, 18.68.

5-(2,4-Dichlorobenzylidene)-3-phenyl-2-thioxo-thiazolidin-4-one (2g): Yield 84 %, m.p. 218-220 ºC; IR (KBr, ν_{max}, cm^{-1}): 3246, 3034, 2946, 1716. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 6.93 (CH=$C_{5\text{-thiazolidinone}}$), 7.10 (s, 1H), 7.14 (s, 1H), 7.18 (d, 2H, *J* = 5.6 Hz), 7.26 (d, 2H, *J* = 6.7 Hz), 7.64 (d, 2H, *J* = 7.3 Hz), 7.64-7.14 (8 H, aromatic protons). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 120.0, 120.4, 123.5, 124.1, 127.1, 128.7, 138.2, 141.0, 142.0 (CH=$C_{5\text{-thiazolidinone}}$), 147.6, 163.8 (C=O), 193.0 (C=S). MS m/z: 364.95 (M + 1), 219, 157, 143, 77. Anal.: $C_{16}H_9Cl_2NOS_2$ (366.28); calcd. (%): C, 52.46; H, 2.48; N, 3.82; O, 4.37; S, 17.51. Found (%): C, 52.43; H, 2.52; N, 3.80; O, 4.33; S, 17.53.

5-(4-Ethoxybenzylidene)-3-phenyl-2-thioxo-thiazolidin-4-one (2h): Yield 85 %, m.p. 226-228 ºC; IR (KBr, ν_{max}, cm^{-1}): 3248, 3036, 2944, 1716, 1591. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.98 (t, 3H, CH_3), 3.98 (d, 2H, CH_2), 6.78 (CH=$C_{5\text{-thiazolidinone}}$), 7.08 (s, 1H), 7.19 (d, 2H, *J* = 6.3 Hz), 7.20 (d, 2H, *J* = 5.5 Hz), 7.28 (d, 2H, *J* = 7.3 Hz), 7.12-7.64 (9 H, aromatic protons), 7.70 (d, 2H, *J* = 6.7 Hz). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 77, 120.0, 120.4, 121, 123.5, 124.1, 127.1, 128.7, 138.2, 141.0, 142.0 (CH=$C_{5\text{-thiazolidinone}}$), 147.6, 163.8 (C=O), 193.0 (C=S). MS m/z: 341.05 (M + 1), 219, 155, Anal.: $C_{18}H_{15}NO_2S_2$: (341.45): Calcd. (%): C, 63.32; H, 4.43; N, 4.10; O, 9.37; S, 18.78; found (%): C, 63.30; H, 4.41; N, 4.08; O, 9.34; S, 18.76.

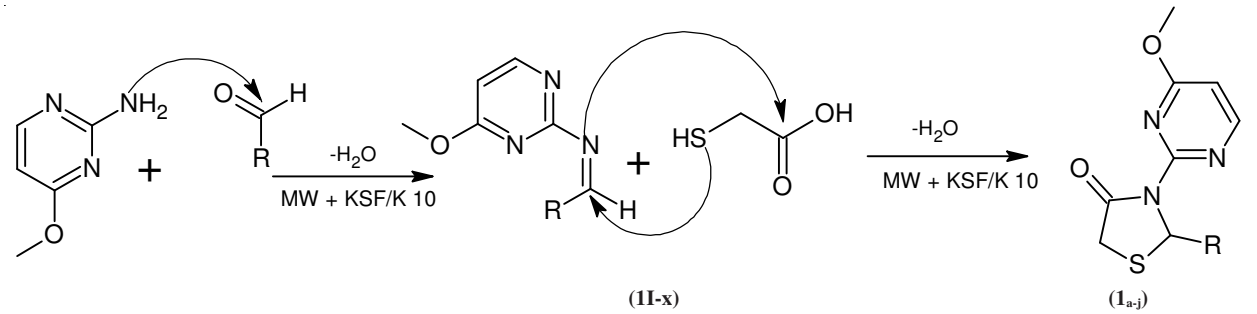
5-[2-(Furan-2-yl)benzylidene]-3-phenyl-2-thioxo-thiazolidin-4-one (2i): Yield 96 %, m.p. 210-212 ºC; IR (KBr, ν_{max}, cm^{-1}): 3268, 3024, 2938, 1714, 1595. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 6.30 (m, 3H, C_4H_3O), 6.76 (CH=$C_{5\text{-thiazolidinone}}$), 7.14 (s, 1H), 7.16 (d, 2H, *J* = 6.3 Hz), 7.24 (d, 2H, *J* = 5.7 Hz), 7.42 (d, 2H, *J* = 6.5 Hz), 7.14-7.66 (9H, aromatic protons), 7.74 (d, 2H, *J* = 7.7 Hz). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 120.0, 120.4, 123.5, 124.1, 127.1, 128.7, 138.2, 141.0, 142.0 (CH=$C_{5\text{-thiazolidinone}}$), 147.6, 163.8 (C=O), 193.0 (C=S). MS m/z: 363.04 (M + 1), 207, 156, 67; Anal.: $C_{20}H_{13}NO_2S_2$: (363.45): calcd. (%): C, 66.09; H, 3.61; N, 3.85; O, 8.80; S, 17.64; found (%): C, 66.05; H, 3.59; N, 3.82; O, 8.78; S, 17.62.

5-(2,4-Difluorobenzylidene)-3-phenyl-2-thioxo-thiazolidin-4-one (2j): Yield 86 %, m.p. 208-210 ºC; IR (KBr, ν_{max}, cm^{-1}): 3264, 3034, 2948, 1714, 1173. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.00 (s, 1H), 7.24 (d, 2H, *J* = 6.3 Hz), 7.48 (CH=$C_{5\text{-thiazolidinone}}$), 7.54 (d, 2H, *J* = 5.6 Hz), 7.64 (d, 2H, *J* =7.2 Hz), 8.14 (d, 2H, *J* = 7.7Hz). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 120.0, 120.4, 123.5, 124.1, 127.1, 128.7, 138.2, 141.0, 142.0 (CH=$C_{5\text{-thiazolidinone}}$), 147.6, 163.8 (C=O), 193.0 (C=S). MS m/z: 333.01 (M + 1), 219, 126, 77. Anal.: $C_{16}H_9F_2NOS_2$: (333.37): Cald. (%): C, 57.64; H, 2.72; N, 4.20; O, 4.80; S, 19.24. found (%): C, 57.62; H, 2.68; N, 4.16; O, 4.82; S, 19.23.

RESULTS AND DISCUSSION

First step, substituted benzaldehydes were reacted with 4-methoxypyrimidin-2-amine and the mixture was subjected to microwave irradiation to form Schiff bases as intermediate products. The intermediate products were further treated with thioglycolic acid/mercaptoacetic acid under microwave radiation to form 4-thiazolidinone derivatives and recrystallized from ethanol. Reactions were carried out in the four controlled variables power 200 watt, temperature 95 ºC, stirring speed 250 rpm and time 10-14 min (**Scheme-I**).

Environmentally benign solid phase catalysts (montmorilinite clays; K10 and KSF) were used to prepare the novel compounds of series (**1$_{a-j}$**). The final products were identified by FTIR, ^{1}H and ^{13}C NMR. In FTIR spectra peaks which appeared at 1715 and 1614 cm^{-1} due to thiazolidinone, C=O and C=N, respectively. In compounds **1d** and **1i** Ar-OH bands displayed bands at 3346-3331 cm^{-1} and bands of Ar-F were displayed in the range 1145-1130 cm^{-1} for the compounds **1h**. In ^{1}H NMR (300 MHz, $CDCl_3$) δ a signal at 8.90 ppm for one proton (pyrimidine), 6.75-6.82 multiplet of three protons on aromatic [$(C_4H_3(CH_3)_2$], signal appearing at 5.92 ppm indicated the presence one proton (s, H, $C_{2\text{-thiazolidinone}}$), a singlet appear at



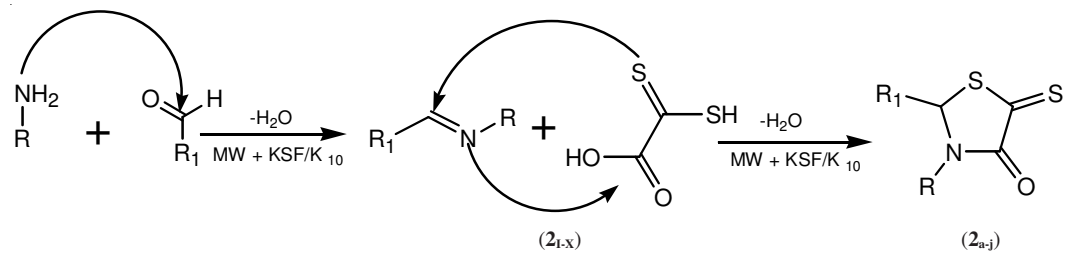
Scheme-I: Reaction between 5-methoxypyrimidin-2-amine and benzaldehyde (**1I-x**) and mercaptoacetic acid to form compounds of thiazolidin-4-ones (**1a-j**)

Compound	(R)	Compound	(R)
1a	2,5-Dimethylbenzaldehyde	**1f**	4-(Dimethylamino)benzaldehyde
1b	4-Ethylbenzaldehyde	**1g**	2,5-Dichlorobenzaldehyde
1c	4-Methoxybenzaldehyde	**1h**	2,5-Difluorobenzaldehyde
1d	2-Hydroxy-5-methoxybenzaldehyde	**1i**	2,5-Dihydroxybenzaldehyde
1e	4-Ethoxybenzaldehyde	**1j**	3-(Furan-2-yl)benzaldehyde

3.73 ppm for three protons (s, 3H, OCH_3), at 3.38 confirmed the presence of two protons (d, 2H, $C_{5\text{-thiazolidinone}}$) and signal appeared at 2.35 for six protons of $(CH_3)_2$ on phenyl. On the other hand ^{13}C NMR signal were recorded at 171.2 (C=O thiazolidinone), 59.4 ($C_{2\text{-thiazolidinoe}}$), 33.6 ($C_{5\text{-thiazolidinoe}}$) and 17.4 ($CH_3$). Final confirmation was made by mass spectrometer, m/z (%): 315 ($C_{16}H_{17}N_3O_2S$), 211 ($C_8H_9N_3O_2S$), 207 ($C_{11}H_{13}NOS$), 106 (C_8H_{10}) and elemental analysis.

2-(2,5-Dimethylphenyl)-3-(4-methoxypyrimidin-2-yl)-thiazolidin-4-one (1a): The compounds **1a**, **1b**, **1c**, **1g** and **1i** in the presence of solid phase catalysts which were obtained in better yields than the compounds synthesized without solvent (reaction medium). In the conventional methods such reactions require longer reaction times and use toxic solvents (pyridine, dimethyl formamide, dimethyl sulphoxide, dry benzene *etc.*) with a considerable amount of catalyst[22,23]. The combination of microwave and solid phase catalyst considerably enhanced reaction rate, provided cleaner products and simplified the whole process under non polluted conditions. It is pertinent to mention that the present reactions under microwave radiation dramatically reduce the reaction time from 12-24 h (conventional method) to a few minutes and data for the same are shown in Table-1.

A second series of 4-thiazolidinone derivatives (**2a-j**) were prepared by using two methods microwave procedure-I: Multi-component reaction using montmorillonite clays (KSF and K-10) and Microwave procedure-II: Solvent free, multi-component reaction and it was found that first was better in yield ranging from 79-96 % while yield in procedure-II ranging from 35-79 %. In this series; sulfanyl(thioxo)acetic acid was treated with Schiff base followed by condensation reaction of substituted aromatic amines with substituted aromatic aldehydes under microwave irradiation coupled with solid phase catalysts (K-10 and KSF types). When a mixture of sulfanyl(thioxo)acetic acid, aromatic amine and substituted aromatic aldehyde was irradiated in a microwave, the reaction completed in 10-12 min. The reaction mixture was then washed with a small amount of ethanol. The crude products were purified by recrystallization from ethanol to afford products with good yields (79-96 %). The results for the synthesis of these compounds are given in Table-2. The microwave with K-10 (montmorillonite catalyst) showed excellent results then other procedure in this study. The compounds **2a**, **2b**, **2c**, **2d** and **2i** were synthesized in good yield 88, 89, 90, 93 and 96, respectively with procedure-I and K-10.



Scheme-II: Hypothesized formation mechanism of the thiazolidin-4-ones (**2a-j**) with KSF and K10

Compound	(R)	Compound	(R)
2a	Benzaldehyde	**2f**	4-Nitrobenzaldehyde
2b	4-Methylbenzaldehyde	**2g**	2,4-Dichlorobenzaldehyde
2c	4-Methoxybenzaldehyde	**2h**	4-Ethoxybenzaldehyde
2d	3-Hydroxy-4-methoxybenzaldehyde	**2i**	2-(Furan-2-yl)benzaldehyde
2e	4-(Dimethylamino)benzaldehyde	**2j**	2,4-Difluorobenzaldehyde

TABLE-1
PERCENTAGE YIELD AND TIME OF CONVENTIONAL AND NON CONVENTIONALPROCEDURES

S. No.	Conventional method		Non-conventional methodyield (%)			
	Yield (%)	Time(h)	SMCR*	MCR** with KSF	MCR** withK-10	Time(min)
1a	44	12	54	80	92	10
1b	43	18	39	79	91	14
1c	44	12	45	84	90	12
1d	47	16	65	86	94	12
1e	40	16	39	83	90	14
1f	43	18	46	74	79	14
1g	40	20	62	78	87	12
1h	41	12	55	89	83	12
1i	34	24	34	85	94	14
1j	38	16	35	69	83	10

**MCR with K-10 and KSF =Microwave procedure-I: Multi-component reaction using montmorillonite clays (K-10and KSF). *SMCR= Microwave procedure-II: Solvent free, Multi-component reaction.

TABLE-2
PERCENTAGE YIELD COMPARISON BETWEEN CONVENTIONAL AND NON-CONVENTIONAL PROCEDURES

S. No.	Conventional method		Non-conventional methodyield (%)			
	Yield (%)	Time(h)	SMCR*	MCR** with KSF	MCR** withK-10	Time(min)
2a	44	06	36	78	88	12
2b	43	06	79	81	89	12
2c	44	06	40	80	90	12
2d	47	06	46	84	93	12
2e	40	06	56	82	94	10
2f	42	08	51	72	79	10
2g	40	08	35	71	84	12
2h	40	08	68	76	86	10
2i	35	08	58	84	96	10
2j	37	08	68	79	86	12

**MCR with K-10 and KSF =Microwave procedure-I: Multi-component reaction using montmorillonite clays (K-10and KSF). *SMCR= Microwave procedure-II: Solvent free, Multi-component reaction.

The IR spectra showed absorption bands in the range 1720-1714 cm^{-1} due to the presence of C=O of 4-thiazolidinone (**2a-j**), absorption bands around 3360-3340 cm^{-1} due to the presence of hydroxyl group (**2d**) and 1173 cm^{-1} for flouro group (**2j**), respectively. The ^1H NMR spectra the compound (**2a**) showed peaks in the range 7.58-7.04 ppm due to aromatic protons clustered in this region. The singlet appeared at 6.80 ppm of one proton (CH = thiazolidinone). The detailed ^1H NMR data of each compound is presented at the end. In ^{13}C NMR spectra, signals were recorded at 193.5 (C=S, thiazolidinone) 166.9 (C=O thiazolidinone), 142 (C = thiazolidinone), 115.9 (CH=C thiazolidinone), while rest of the carbon atoms produced peaks regarding their environment. Molecular ion peak for compound **2a** at m/z 297 confirmed the molecular weight of corresponding compound. The mass spectra of rest of the compounds (**2a-j**) showed molecular ion peaks corresponding to their molar masses. The fragmentation pattern was 219, 206, 143, 90 and 77. The elemental analysis data also corresponded to the proposed formula.

Multi-component reaction using montmorillonite clays (K-10 and KSF) provided consistent yield. Because mineral oxides (SPC) are good microwave adsorbents and result in very rapid and homogenous heating and less degradation of final products as compared to conventional heating. This method is more advantageous towards environment because SPC (K-10 and KSF) can be reused after washing with ethanol. Moreover the separation of final products and catalysts is easy. High yields were obtained with K-10 from rest of all procedures and 10 % less yield was obtained with KSF as compared with K-10.

Antibacterial activity *in vitro* of compounds Ia-j and 2a-j: The effects of newly synthesized 4-thiazolidinone analogues were studied against nine bacterial strains and data is presented in Table-3. The activities against gram negative bacterial strains of 1st series of 4-thiazolidinone derivatives (**Ia-j**) were good but the compounds of 2nd series (**2a-j**) had not shown better result. First series showed better results due to presence of pyrimidine molecule and second series showed better results against gram positive bacterial strains due to presence of more sulfur atoms in basic structure. From the data obtained (Table-3), the compounds **1h** and **2j** exhibited high activity against negative bacterial strains as compared to the other compounds of these two series. These compounds (**1h** and **2j**) showed high activity due to the presence of highest electronegative group. The compounds **1f** and **2e** exhibited high activity against gram positive bacterial strains under study. The substituted dimethyl amino group was found to increase the zone of inhibition against gram positive bacterial strains *S. aureus* and *B. subtilis* (**1f** and **2e**). The substituted methoxy, ethoxy and hydroxyl groups participated a little in the zone of inhibition against the gram positive bacterial growth as shown in Table-3 for the compounds **1c**, **1d**, **1e**, **1i**, **2c**, **2d** and **2h**. Other substituents *i.e.*, methanol and benzene did not affect the zone of inhibition against the most of bacterial strains under study. In general, 4-thiazolidinone derivatives showed different activities due to the presence of different groups. The compounds

TABLE-3
ANTIBACTERIAL RESPONSE OF COMPOUNDS **Ia-j** AND **2a-j**

Comp. No.	Antibacterial activity of compounds **Ia-j** and **2a-j**								
	Gram positive				Gram negative				
	S. aureus	*B. subtilis*	*B. pumilus*	*L. monocytogenes*	*E. coli*	*S. typhi*	*P. aeruginosa*	*P. vulgaris*	*P. Shigella*
1a	–	–	–	–	+	+	+	+	–
1b	–	–	–	–	+	+	+	+	–
1c	+	+	–	–	+	+	+	+	–
1d	+	+	+	–	+	+	+	+	–
1e	+	+	–	–	+	+	+	+	–
1f	++	++	+	+	++	++	+	+	–
1g	++	++	++	–	++	++	+	+	–
1h	+	–	–	–	+++	+++	++	+	+
1i	+	+	–	+	++	++	++	+	++
1j	–	–	–	–	+	+	+	++	++
2a	+	+	+	–	–	–	–	–	–
2b	+	+	+	–	–	–	–	–	–
2c	+	+	+	–	–	+	–	–	–
2d	++	++	+	+	+	+	–	–	–
2e	++	++	++	++	+	+	–	–	–
2f	++	+	++	+	–	–	–	–	–
2g	++	++	++	+	+	+	–	–	–
2h	+	+	+	+	–	–	–	–	–
2i	+	+	+	+	–	–	–	+	+++
2j	+++	+++	++	+	++	++	+	–	–
CIP.	+++	+++	++	–	++	+++	+++	+	+
SMZ	++++	+++	+++	–	++	+++	++	+	+

Highly active=++++(inhibition zone > 20 mm). Highly active=+++ (inhibition zone 15-20 mm). Active=++ (inhibition zone 10-15 mm). Slightly active=+ (inhibition zone 5-10 mm). Inactive= – (inhibition zone <5mm). Reference standards. CIP=Ciprofloxacin. SMZ=Sulphamethoxazole.

1h and **2j** showed excellent results due to the presence of fluoro group; the compounds **1g** and **2g** showed significant results against *S. aureus* and *B. subtilis* due to the presence of chloro group and the compounds **1j** and **2i** produced good results against *P. vulgaris* and *P. shigella* due to the presence of furan group. The basic molecule of 2nd series showed almost similar behaviour as shown by standard drug sulfamethoxazole due to the presence of more sulfur content. The groups 4-methoxy, methyl and ethoxy did not have significant effect on the inhibition of bacterial growth. Ciprofloxacin and sulphamethoxazole were used as reference standard for comparison with synthesized compounds. The results of two series are presented in Table-3.

Conclusion

Eco-friendly approaches *i.e.*, solvent free, multi-component reaction, multi-component reaction using montmorillonite clays (K-10 and KSF) coupled with microwave radiation were tried. These approaches have many distinct advantages that are easy separation, consistent yield, minimal environmental effects, recyclability of catalysts and elimination of solvents thereby preventing pollution in organic synthesis 'at source'. The present results demonstrate that montmorillonite K-10 is more efficient than KSF.

The synthesized compounds were tested for antibacterial activity and showed very promising results with positive activity as compared with standard reference drugs. Compounds **1f**, **1**h, **2e** and **2j** exhibited better inhibition as compared to reference drugs. The compounds **2d**, **2e**, **2f** and **2g** are viable alternatives to existing sulfonamides. Compounds **1f**, **1g**, **2d**, **2d** and **2g** also showed inhibition against *S. aureus* and *B. subtilis* hence it may be used for the cure of *S. aureus* and *B. subtilis* infection.

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