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Microwave-Assisted Synthesis, Characterization and Antimicrobial Potencies of N-Substituted Iminothiazodin-4-One Derivatives

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ABSTRACT

The biggest and most multifaceted class of organic compounds includes heterocyclic compounds. Currently, several heterocyclic compounds are identified, and persistently gratefulness to tremendous synthetic work and synthetic usefulness, the number is increasing exponentially. In most fields of science, including medicinal, pharmaceutical, and agro-chemistry, heterocyclic compounds have a function, and biochemistry is also another area. In this research article, the green approach is administered for achieving the nitrogen, oxygen and sulphur centered five-membered heterocyclic derivatives. By taking the whole thing in to account of hetero-chemistry, the moderately effective analog for gram-positive and gram-negative bacterial strains was shown for the five-membered heterocyclic compound series of N-substituted iminothiazodine-4-one and N-(benzylideneamino)thiazol-4(5H). Throughout the synthesized series of the compound 6c revealed very much active potent against the gram-negative Escherichia coli bacterial strain and the compound 6b point out moderately active against the gram-positive Bacillus subtilis bacteria strains in accordance with the standard drug. The 5a and 6a compounds showed very strong activity against the fungal strain of *Candida albicans* and 6b as well as 6c were more active and highly potent than the standard drugs against *Aspergillus niger* species. In the view of this research drive states that all the synthesized compounds might be used for the development for further heterocyclic entities.

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INTRODUCTION

The creation and discovery of new physiologically and pharmacologically effective substances include heterocyclic compounds, including nitrogen and sulphur. Therapeutic value molecules are designed, synthesized and produced for medicinal chemistry. The development of various privileged systems of proven utility in medicinal chemistry has been the result of progress in areas such as combinatorial chemistry and heterocyclic chemistry in the last several decades (Verma and Saraf, 2008). Most of the ring systems derived by the replacement of a methane group with a nitrogen atom are formally

derived from pyrrole, furan, and thiophene. It is the shift in nitrogen location, contributing to the structural heterogeneity of the heterocycle community. The heteroatoms, such as oxygen in isoxazoles, oxazoles, oxadiazoles, or isothiazoles, thiadiazoles, sulphide can be contained in aromatic nitrogen-containing heterocycles with five members. Heterocyclic compounds are very common in nature. Throughout the majority of the identified organic compounds tend to be heterocyclic. Five-member aromatic ring heterocycles are widely distributed in nature and are often important in different biochemical processes. The bio-isosteres of several substituents are also hetero-aromatic rings, including phenyl rings and carboxyl and their ester analogs, thus rendering the resulting substances more medicinal. As a result, medicinal chemists are usually included in new chemical entities (Dalvie *et al.*, 2002; Patani *et al.*, 1996).

Thiazolidinone (Kasmi-Mir *et al.*, 2006; Zhou *et al.*, 2008), a fourth carbon saturated carbonyl thiazole the band is considered a mystical activity with virtually all kinds of biological activities. It is part of a significant group of sulfur and nitrogen-containing heterocyclic compounds in a five-part loop (Patel *et al.*, 2015). This biologically active scaffold fostered curiosity in synthesizing many new compounds utilizing several substitutions at different positions connected to 4-thiazolidinone moieties substitution at 2, 3 and 5 levels. The substituent at 2-, 3-and 5-positions can vary, but the group attached to the carbon atom in 2-position exerts the greatest difference in structure and properties (Mistry and Desai, 2004). Thaiazole tetrahydro derivative is known as thiazolidine, and thiazolidine is known as thiazolidinone. Many halogen-substituted monocyclic α-lactams have powerful antibacterial, antimicrobial (Jubie *et al.*, 2009), anti-inflammatory (Yerigeri *et al.*, 2008), anticonvulsant and anti-tubercular activity. These also act as enzyme inhibitors and influence the central nervous system. 4-thiazolidinone and 2-azetidinone derivatives are essential in medicinal chemistry, as they exhibit a range of microbiological behavior. In recent times, 2-aryl-4-thiazolidinone has been synthesized to demonstrate powerful selective anti-platelet triggering 538 mechanisms, both in vitro and in vivo and anti-inflammatory (Sayyad *et al.*, 2006), antibacterial (Colombo *et al.*, 2008), anticancer (Murugesan *et al.*, 2009) and anti-HIV-1 activity (Patai, 1970). In the view of these useful biological activities, pharmacological properties of iminothiazodin-4-one derivatives and the importance of microwave-assisted technique various methods have been developed for their synthesis.

MATERIALS AND METHODS

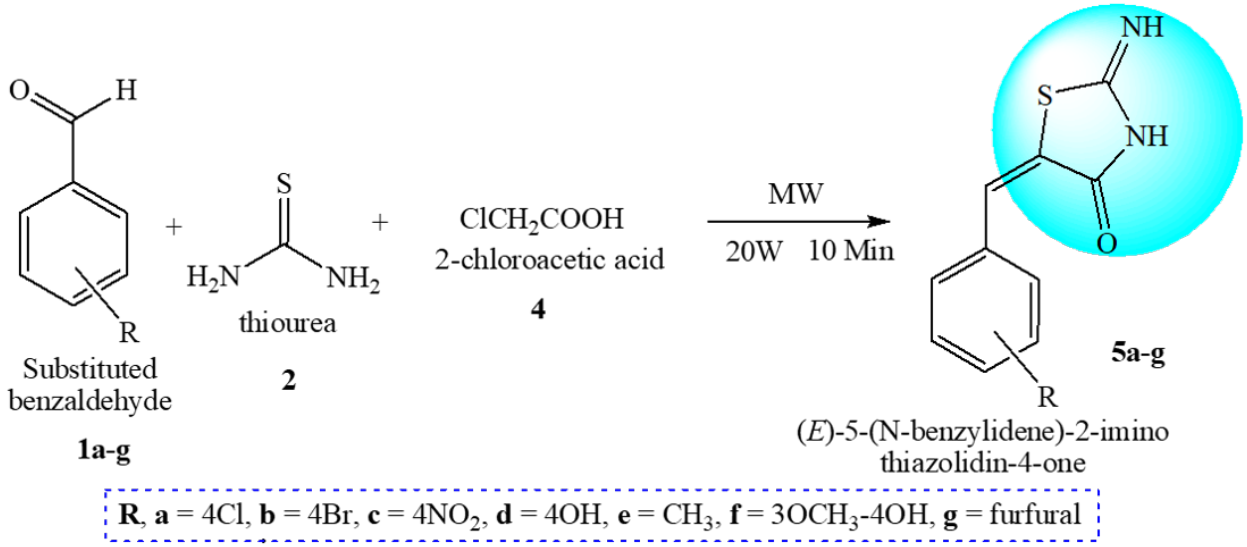
Melting points were recorded in open glass capillaries and were uncorrected. IR spectra in (KBr pallets) were verified on Shimadzu FTIR-8400S and ATR Brucker alpha FT-IR spectrophotometer. ^{13}C NMR and ^{1}H NMR spectra were recorded on 400.13 MHz by Brucker spectrophotometer. The NMR prediction reference values were stated from the reference books (Pavia *et al.*, 2008; Silverstein *et al.*, 2005). The reaction was monitored by thin-layer chromatography, which was performed by using precoated silica gel aluminium plates run in the solvent benzene. All the compounds 5a-g and 6a-g were synthesized in the domestic microwave oven Samsung in hours from the corresponding commercially purchased and available 4-hydroxy-3-methoxy benzaldehyde (vanillin), furfural, 4-chloro benzaldehyde, 4-bromo benzaldehyde, 4-nitro benzaldehyde, 4-hydroxy benzaldehyde, 4-methyl benzaldehyde, chloroacetic acid, thiourea, citric acid and ethanol. Antimicrobial screening the gram-positive bacteria *Bacillus subtilis* (NCIM-2921), gram-negative bacteria *Escherichia coli* (NCIM-2109), *Candida albicans* (NCIM 3471) and *Aspergillus niger* (NCIM 545) were purchased from National Collection of Industrial Microorganisms, National Chemical Laboratory (NCL), Pune, MH, India. Amphotericin-B, Chloramphenicol, and Dimethylsulfoxide (DMSO) solvent were used for the antimicrobial assay.

Synthesis of N-substituted iminothiazodin-4-one derivatives (5a-g)

The substituted (E)-5-(4-N-benzylidene)-2-iminothiazolidin-4-one (5a-g) are synthesized by the mixture of 1 mole of substituted benzaldehyde (1a-g) and 1 mole of thiourea (2) in 1.2 mole of 2-chloro acetic acid under microwave-assisted solvent-free conditions at 20W powers for 5-10 minutes. The synthesized compounds were recovered and recrystallized by ethanol (Scheme 1).

(E)-5-(4-chlorobenzylidene)-2-iminothiazolidin-4-one(5a)

M. F.: $C_{10}H_7ClN_2OS$; Colour: Pale yellowish solid; M. Wt.: 238; % Yield: 66.90%; M.P. (ºC): 194-196 ºC; Elemental: C, 49.80; H, 3.11; N, 12.16; FTIR: γ-lactam C=O: 1680 cm^{-1}, stretching C=C in α,β ketone: 1590 cm^{-1}, tri-substituted bending for C=C: 820 cm^{-1}, cyclic aromatic ring C=C (3-peaks): 1425 cm^{-1}, 1490 cm^{-1} and 1509 cm^{-1}, aromatic compound C-H overtone: 2050 cm^{-1}, imine C=N stretching: 1715 cm^{-1}, aldehyde C-H: 1367 cm^{-1}, stretching of N-H: 2980 cm^{-1}, 2° amine bending N-H: 3190



Scheme 1: Synthesis of Substituted iminothiazolidin-4-one

cm^{-1}, Ar-Cl: 594 cm^{-1}, ^1H NMR: δ (ppm): 8.12-8.01 (m, 4H, Ar), 10.02 (s, 1H, =CH), 4.85 (s, 2H, -NH)

(E)-5-(4-bromobenzylidene)-2-iminothiazolidin-4-one(5b)

M. F.: $C_{10}H_7BrN_2OS$; Colour: Pale yellowish solid; M. Wt.: 283.14; % Yield: 52.75%; M. P. (ºC): 215-217 ºC; Elemental: C, 50.21; H, 3.21; N, 11.26; FTIR: γ-lactam C=O: 1673 cm^{-1}, stretching C=C in α,β ketone: 1588 cm^{-1}, tri-substituted bending for C=C: 818 cm^{-1}, cyclic aromatic ring C=C (3-peaks): 1372 cm^{-1}, 1487 cm^{-1} and 1511 cm^{-1}, aromatic compound C-H overtone: 2050 cm^{-1}, imine C=N stretching: 1739 cm^{-1}, aldehyde C-H: 1372 cm^{-1}, stretching of N-H: 2980 cm^{-1}, 2° amine bending N-H: 3198 cm^{-1}, Ar-Br: 518 cm^{-1}, ^1H NMR: δ (ppm): 8.55-8.21 (m, 4H, Ar), 9.98 (s, 1H, =CH), 5.02 (s, 2H, -NH)

(E)-2-imino-5-(4-nitrobenzylidene)thiazolidin-4-one(5c)

M. F.: $C_{10}H_7N_3O_3S$; Colour: Whitish yellowish solid; M. Wt.: 249.25; % Yield: 65.62%; M. P. (ºC): 270-272 ºC; Elemental: C, 49.28; H, 3.05; N, 17.26; FTIR: γ-lactam C=O: 1675 cm^{-1}, stretching C=C in α,β ketone: 1579 cm^{-1}, tri-substituted bending for C=C: 846 cm^{-1}, cyclic aromatic ring C=C (3-peaks): 1488 cm^{-1}, 1528 cm^{-1} and 1579 cm^{-1}, aromatic compound C-H overtone: 2050 cm^{-1}, imine C=N stretching: 1711 cm^{-1}, aldehyde C-H: 1394 cm^{-1}, stretching of N-H: 2981 cm^{-1}, 2° amine bending N-H: 3486 cm^{-1}, Ar-NO_2: 1528 cm^{-1}, ^1H NMR: δ (ppm): 8.42-8.08 (m, 4H, Ar), 10.17 (s, 1H, =CH), 4.14 (s, 2H, -NH)

(E)-5-(4-hydroxybenzylidene)-2-iminothiazolidin-4-one(5d)

M. F.: $C_{10}H_8N_2O_2S$; Colour: Dark brown solid; M. Wt.: 220.25; % Yield: 47.22%; M. P. (ºC): 231-233 ºC; Elemental: C, 52.98; H, 3.45; N, 12.02; FTIR: γ-lactam C=O: 1669 cm^{-1}, stretching C=C in α,β ketone: 1653 cm^{-1}, tri-substituted bending for C=C: 818 cm^{-1}, cyclic aromatic ring C=C (3-peaks): 1488 cm^{-1}, 1509 cm^{-1} and 1579 cm^{-1}, aromatic compound C-H overtone: 1816 cm^{-1}, imine C=N stretching: 1721 cm^{-1}, aldehyde C-H: 1376 cm^{-1}, stretching of N-H: 2981 cm^{-1}, 2° amine bending N-H: 3426 cm^{-1}, Ar-NO_2: 1528 cm^{-1}

(E)-2-imino-5-(4-methylbenzylidene)thiazolidin-4-one(5e)

M. F.: $C_{11}H_{10}N_2OS$; Colour: Yellow solid; M. Wt.: 218.27; %Yield: 25.51%; M. P. (ºC): 211-213 ºC; Elemental: C, 59.99; H, 4.15; N, 12.42; FTIR: γ-lactam C=O: 1827 cm^{-1}, stretching C=C in α,β ketone: 1721 cm^{-1} , tri-substituted bending for C=C: 805 cm^{-1}, cyclic aromatic ring C=C (3-peaks): 1510 cm^{-1}, 1599 cm^{-1} and 1669 cm^{-1}, aromatic compound C-H overtone: 2050 cm^{-1}, imine C=N stretching: 1744 cm^{-1}, aldehyde C-H: 1392 cm^{-1}, stretching of N-H: 2980 cm^{-1}, 2° amine bending N-H: 3423 cm^{-1}, Ar-CH_3: 1446 cm^{-1}

(E)-5-(4-hydroxy-3-methoxybenzylidene)-2-iminothiazolidin-4-one(5f)

M. F.: $C_{11}H_{10}N_2O_3S$; Colour: Brown solid; M. Wt.: 250.27; % Yield: 25.60%; M.P. (ºC): 240-242 ºC; Elemental: C, 53.09; H, 4.19; N, 11.59; FTIR: γ-lactam C=O: 1827 cm^{-1}, stretching C=C in α,β ketone: 1722 cm^{-1} , tri-substituted bending for C=C: 804 cm^{-1}, cyclic aromatic ring C=C (3-peaks): 1447 cm^{-1}, 1515 cm^{-1} and 1580 cm^{-1}, aromatic compound C-H overtone: 2014 cm^{-1}, imine C=N stretching: 1668 cm^{-1}, aldehyde C-H: 1395 cm^{-1}, stretching of N-H:

2980 cm^{-1}, 2° amine bending N-H: 3462 cm^{-1}, Ar-OCH_3: 1286 cm^{-1}, Ar-OH: 2898 cm^{-1}

(E)-5-(furan-2-ylmethylene)-2-iminothiazolidin-4-one(5g)

M.F.: $C_8H_6N_2O_2S$; Colour: Carbon black solid; M.Wt.: 194.21; % Yield: 25.86%; M.P. (ºC): >320 ºC; Elemental: C, 49.09; H, 3.54; N, 14.79; FTIR: γ-lactam C=O: 1826 cm^{-1}, stretching C=C in α, β ketone: 1722 cm^{-1} , tri-substituted bending for C=C: 811 cm^{-1}, cyclic ring C=C (2-peaks): 1518 cm^{-1} and 1598 cm^{-1}, cyclic compound C-H overtone: 1980 cm^{-1}, imine C=N stretching: 1669 cm^{-1}, aldehyde C-H: 1393 cm^{-1}, stretching of N-H: 2981 cm^{-1}, 2° amine bending N-H: 3487 cm^{-1}

Synthesis of N-(benzylideneamino)thiazol-4(5H)-one derivatives (6a-g)

The substituted N-(benzylideneamino)thiazol-4(5H)-one (6a-g) derivatives were synthesized by the mixture of 0.01mole of previously prepared N-substituted iminothiazodin-4-one (5a-g) compounds and 0.01 mole of substituted aromatic aldehydes (1a-g) in 2 gm of citric acid under microwave-assisted solvent-free conditions on 40 W powers for 3-5 minutes. The afforded coloured compounds were recovered and recrystallized by ethanol (Scheme 2).

(5Z)-5-(4-chlorobenzylidene)-2-((4-chlorobenzylidene)amino)thiazol-4(5H)-one (6a)

M. F.: $C_{17}H_{10}Cl_2N_2OS$; Colour: Yellow Solid; M. Wt.: 361.25; % Yield: 53.18%; M. P. (ºC): 296-298 ºC; Elemental: C, 57.02; H, 2.29; N, 6.66; FTIR : γ-lactam C=O: 1826 cm^{-1}, stretching C=C in α,β ketone: 1714 cm^{-1} , tri-substituted bending for C=C: 819 cm^{-1}, cyclic aromatic ring C=C (3-peaks): 1560 cm^{-1}, 1590 cm^{-1} and 1611 cm^{-1}, aromatic compound C-H overtone: 1890 cm^{-1}, imine C=N stretching: 1669 cm^{-1}, aldehyde C-H: 1378 cm^{-1}, stretching of N-H: 2981 cm^{-1}, 2° amine bending N-H: 3433 cm^{-1}, Ar-Cl: 819 cm^{-1}, ^{1}H NMR: δ (ppm): 7.98-7.78 (m, 8H, Ar), 10.27 (s, 2H, =CH)

(5Z)-5-(4-bromobenzylidene)-2-((4-bromobenzylidene)amino)thiazol-4(5H)-one (6b)

M.F.: $C_{17}H_{10}Br_2N_2OS$; Colour: Whitish Orange Solid; M. Wt.: 450.15; % Yield: 65.77%; M.P. (ºC): 154-156 ºC; Elemental: C, 46.08; H, 2.82; N, 7.31; FTIR: - γ-lactam C=O: 1826 cm^{-1}, stretching C=C in α,β ketone: 1704 cm^{-1} , tri-substituted bending for C=C: 817 cm^{-1}, cyclic aromatic ring C=C (3-peaks): 1537 cm^{-1}, 1561 cm^{-1} and 1610 cm^{-1}, aromatic compound C-H overtone: 1888 cm^{-1}, imine C=N stretching: 1654 cm^{-1}, aldehyde C-H: 1378 cm^{-1}, stretching of N-H: 2980 cm^{-1}, 2° amine bending N-H: 3334 cm^{-1}, Ar-Br: 616 cm^{-1}, ^{1}H NMR: δ (ppm): 7.76-7. 76 (m, 8H, Ar), 9.97, (s, 2H, =CH); ^{13}C NMR: δ (ppm): α,β-unsaturated C=O: 191.16, Aromatic ring carbons: 119.92, 122.98, 129.82, 131.00, 131.66, 131.88, C=N: 148.74, 158.73, methane carbon -CH: 132.72, unsaturated carbon (C=C): 135.03

(5Z)-5-(4-nitrobenzylidene)-2-((4-nitrobenzylidene)amino)thiazol-4(5H)-one (6c)

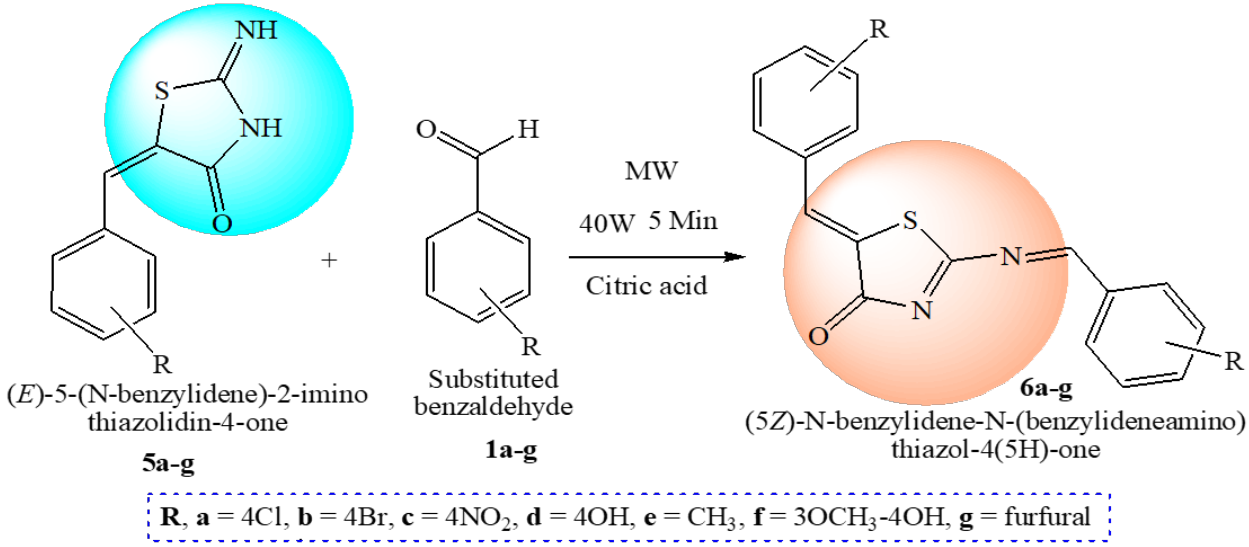
M. F.: $C_{17}H_{10}N_4O_5S$; Colour: Whitish Solid; M. Wt.: 382.35; % Yield: 95.54%; M. P. (ºC): 149-151 ºC; Elemental: C, 53.78; H, 2.22; N, 14.11; FTIR: γ-lactam C=O: 1824 cm^{-1}, stretching C=C in α,β ketone: 1706 cm^{-1} , tri-substituted bending for C=C: 817 cm^{-1}, cyclic aromatic ring C=C (3-peaks): 1562 cm^{-1}, 1606 cm^{-1} and 1610 cm^{-1}, aromatic compound C-H overtone: 1887 cm^{-1}, imine C=N stretching: 1656 cm^{-1}, aldehyde C-H: 1346 cm^{-1}, stretching of N-H: 2981 cm^{-1}, 2° amine bending N-H: 3332 cm^{-1}, Ar-NO_2: 1535 cm^{-1}; ^{1}H NMR: δ (ppm): 8.41-8.07 (m, 8H, Ar), 10.17 (s, 2H, =CH)

(5Z)-5-(4-hydroxybenzylidene)-2-((4-hydroxybenzylidene)amino)thiazol-4(5H)-one (6d)

M.F.: $C_{17}H_{12}N_2O_3S$; Colour: Reddish Brown Solid; M. Wt.: 324.35; % Yield: 42.12%; M.P.(ºC): 278-280 ºC; Elemental: C, 61.98; H, 3.80; N, 14.31; FTIR: γ-lactam C=O: 1827 cm^{-1}, stretching C=C in α,β ketone: 1705 cm^{-1} , tri-substituted bending for C=C: 817 cm^{-1}, cyclic aromatic ring C=C (3-peaks): 1509 cm^{-1}, 1562 cm^{-1} and 1600 cm^{-1}, aromatic compound C-H overtone: 1890 cm^{-1}, imine C=N stretching: 1666 cm^{-1}, aldehyde C-H: 1380 cm^{-1}, stretching of N-H: 2981 cm^{-1}, 2° amine bending N-H: 3317 cm^{-1}, Ar-OH: 3195 cm^{-1}

(5Z)-5-(4-bromobenzylidene)-2-((4-bromobenzylidene)amino)thiazol-4(5H)-one (6e)

M.F.: $C_{19}H_{16}N_2OS$; Colour: Cream yellow flakes; M. Wt.: 320.41; % Yield: 23.59%; M. P. (ºC): 285-287 ºC; Elemental: C, 71.38; H, 5.42; N, 8.39; FTIR : γ-lactam C=O: 1828 cm^{-1}, stretching C=C in α,β ketone: 1708 cm^{-1} , tri-substituted bending for C=C: 804 cm^{-1}, cyclic aromatic ring C=C (3-peaks): 1505 cm^{-1}, 1574 cm^{-1} and 1602 cm^{-1}, aromatic compound C-H overtone: 1888 cm^{-1}, imine C=N stretching: 1668 cm^{-1}, aldehyde C-H: 1371 cm^{-1}, stretching of N-H: 2980 cm^{-1}, 2° amine bending N-H: 3332 cm^{-1}, Ar-CH_3: 1371 cm^{-1}, ^{1}H NMR: δ (ppm): 7.84-7.69 (m, 8H, Ar), 9.10, (s, 2H, =CH); ^{13}C NMR: δ (ppm): α,β-unsaturated C=O: 197.02, Aromatic ring carbons: 120.42, 121.91, 128.33, 130.24, 131.01,



Scheme 2: Synthesis of Substituted N-(benzyli deneamino)thiazol-4(5H)-one

132.08, C=N: 150.71, 157.13, methane carbon -CH: 133.12, unsaturated carbon (C=C): 134.67

(5Z)-5-(4-hydroxy-3-methoxybenzylidene)-2-((4-hydroxy-3-methoxybenzylidene) amino)thiazol-4(5H)-one (6f)

M.F.: $C_{19}H_{16}N_2O_5S$; Colour: Brown Solid; M. Wt.: 384.41; % Yield: 40.62%; M.P. (ºC): 268-270 ºC; Elemental: C, 59.75; H,4.11; N, 8.01; FTIR: γ-lactam C=O: 1826 cm^{-1}, stretching C=C in α,β ketone: 1722 cm^{-1} , tri-substituted bending for C=C: 814 cm^{-1}, cyclic aromatic ring C=C (3-peaks): 1581 cm^{-1}, 1599 cm^{-1} and 1655 cm^{-1}, aromatic compound C-H overtone: 1888 cm^{-1}, imine C=N stretching: 1683 cm^{-1}, aldehyde C-H: 1378 cm^{-1}, stretching of N-H: 2980 cm^{-1}, 2° amine bending N-H: 3466 cm^{-1}, Ar-OCH_3: 1253 cm^{-1}, Ar-OH: 3199 cm^{-1}

(5Z)-5-(furan-2-ylmethylene)-2-((furan-2-ylmethylene)amino)thiazol-4(5H)-one (6g)

M.F.: $C_{13}H_8N_2O_3S$; Colour: Brownish black Flakes; M. Wt.: 272.28; % Yield: 59.11%; M.P. (ºC): >320 ºC; Elemental: C, 57.65; H, 2.44; N, 10.40; FTIR: γ-lactam C=O: 1827 cm^{-1}, stretching C=C in α,β ketone: 1721 cm^{-1} , tri-substituted bending for C=C: 798 cm^{-1}, cyclic ring C=C (2-peaks): 1537 cm^{-1} and 1609 cm^{-1}, cyclic compound C-H overtone: 1889 cm^{-1}, imine C=N stretching: 1683 cm^{-1}, aldehyde C-H: 1376 cm^{-1}, stretching of N-H: 2981 cm^{-1}, 2° amine bending N-H: 3403 cm^{-1}

RESULTS AND DISCUSSION

Biological Potencies of (5a-g) and (6a-g)

Antimicrobial Activities of the Synthesized 5a-g and 6a-g Compounds

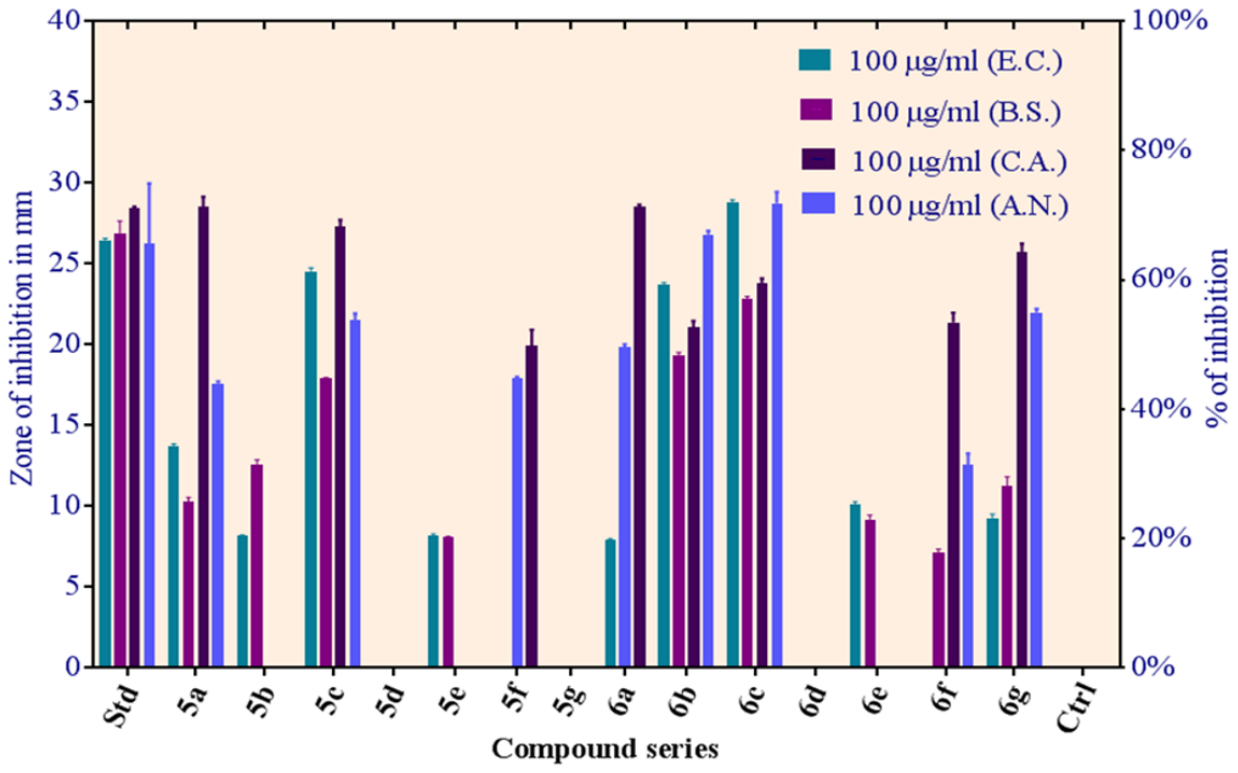
All the synthesized compounds 5a-g and 6a-g from this research paper were evaluated *in-vitro* for antibacterial activity aga*inst bacterial st*rains gram-positive*Bacillus subtil is* and gram-negative *Escherichia coli* at the concentrations of 100μg/mL per disc DMSO *as* a solvent and nutrient agar was employed as culture media. After 48 hrs of incubation at 37ºC, the results were obtainedin the form of clearing zones and were noted after the period of incubation was over. The zones of inhibitions were measured in 'mm' and the data were undertaken in Table 1. Similarly, compounds 5a-g and 6a-g were evaluated *in-vitro* for antifungal activity against fungal strains *Candida albicans and Aspergillus niger* at the concentration 100μg/mL per disc by paper disc diffusion method using DMSO as a solvent. The yeast *Candida albicans* cultured using a malt extract, glucose yeast extract peptone agar medium (MGYP medium) and for fungi, *Aspergillus niger* potato dextrose agar medium was used. After 3-7 days of incubation at 30ºC, the diameters of the zones of inhibition were measured and data is calculated by Mean±SD in Graph 1.

Some of the compound series 5a-g and 6a-g were found considerable active against bacterial strains gram-positive *Bacillus subtilis* and gram-negative *Escherichia coli*. The compound 6c showed highly active potency against the gram-negative *Escherichia coli* bacteria as compared to the standard one and compound 6c revealed moderately active against gram-positive *Bacillus subtilis* bacterial strain as compared to the standard drugs. In the same way, the compounds 5a-g and 6a-g showed superior activity by means of the compounds 5a and 6a showed highly potent activity against *Candida*

Table 1: Antimicrobial activities of 5a-g and 6a-g

Compound Code	Zone diameter in mm against *Escherichia coli* NCIM 2109 (Mean ± SD) 100 μg/mL	Zone diameter in mm against *Bacillus subtilis* NCIM 2921 (Mean ± SD) 100 μg/mL	Zone diameter in mm against *Candida albicans* NCIM 3471 (Mean ± SD) 100 μg/mL	Zone diameter in mm against *Aspergillus niger* NCIM 545 (Mean ± SD) 100 μg/mL
5a	13.70 ± 0.14	10.25 ± 0.29	28.54 ± 0.60	17.61 ± 0.10
5b	8.16 ± 0.04	12.60 ± 0.27	–	–
5c	24.53 ± 0.20	17.91 ± 0.05	27.30 ± 0.40	21.51 ± 0.40
5d	–	–	–	–
5e	8.20 ± 0.08	8.10 ± 0.04	–	–
5f	–	–	19.91 ± 1.00	17.90 ± 0.10
5g	–	–	–	–
6a	7.94 ± 0.05	–	28.54 ± 0.10	19.82 ± 0.20
6b	23.68 ± 0.14	19.34 ± 0.17	21.06 ± 0.40	26.81 ± 0.20
6c	28.77 ± 0.19	22.79 ± 0.18	23.78 ± 0.30	28.72 ± 0.70
6d	–	–	–	–
6e	10.10 ± 0.17	9.18 ± 0.26	–	–
6f	–	7.16 ± 0.17	21.36 ± 0.60	12.57 ± 0.70
6g	9.26 ± 0.24	11.23 ± 0.57	25.72 ± 0.50	21.99 ± 0.20
Ctrl	0.0 ± 0.0	0.0 ± 0.0	0.0±0.0	0.0±0.0
Std	26.43 ± 0.13	26.90 ± 0.75	28.42 ± 0.10	26.26 ± 3.7

SD – Standard Deviation, Ctrl – Control, Std – Standard, '–' means no zone



Graph 1: Antimicrobial activities of 5a-g and 6a-g Mean±SD

albicans fungal strain and 6b and 6c are higher active against *Aspergillus niger* as compare to the standard drugs.

CONCLUSIONS

In the final comment, the five-membered heterocyclic compounds of N-substituted iminothiazodin-4-ones and N-(benzylideneamino)thiazol-4(5H)-one analogs shown to be moderately effective in strains of gram-positive and gram-negative bacteria. Only one compound **6b** proven moderate activity in contrast with the standard one and the compound **6c** showed a highly active bacterial strain against the gram-negative strains, comparing with the standard drugs. Correspondingly, the fungal strains were very effective in almost all compounds. Hence these synthesized compounds could be employed in this specific reference to incorporate further heterocyclic syntheses.

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