



Research Article

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Green synthesis and preliminary pharmacological evaluation of three-substituted thiazide derivatives as antibacterial agents

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ABSTRACT

2-Aminothiazole has great biological and medicinal interest. Some of the marketed drugs also possessed this heterocyclic moiety. This manuscript reports the synthesis of a series of 2-Aminothiazole derivatives. The reaction between secondary amines, benzoyl isothiocyanate, and dialkyl acetylene dicarboxylates (=dialkyl but-2-ynedioates) in the presence of silica gel (SiO_2), led to alkyl 2-(dialkylamino)-4-phenylthiazole-5-carboxylates (6a-6l) in fairly high yields. All title compounds were characterized by IR, NMR and Mass spectroscopy. The antimicrobial activity of the compounds were evaluated against the following microorganisms: *Staphylococcus epidermidis* ATCC.14990, *Bacillus subtilis* ATCC.12711, *Pseudomonas aeruginosa* ATCC 27853, *Staphylococcus aureus* ATCC 25923, *Acinetobacter calcoaceticus* ATCC 23055, and *Escherichia coli* ATCC 25922. The broth macrodilution method was used for determination of the minimum inhibitory concentration (MIC) during preliminary evaluation of antibacterial activity. The compounds yielded MIC values in the range of 7 to 3.9 $\mu\text{g/mL}$ for *Staphylococcus aureus*, 500 to 7 $\mu\text{g/mL}$ for *Staphylococcus epidermidis*, 62.5 to 0.097, for *Bacillus subtilis*, 500 to 125 $\mu\text{g/mL}$, for *Pseudomonas aeruginosa* and 500 to 250 for *Acinetobacter calcoaceticus*. The best MIC value with compounds 6a-6l was obtained for compounds 6e, 6f, 6g and 6h against *Staphylococcus aureus* and *Bacillus subtilis*.

Keywords: Antimicrobial activity; Minimum Inhibitory Concentration; Aminothiazol; antibacterial activity; *In vitro*

INTRODUCTION

The organic moiety containing nitrogen and sulfur atoms are highly effective against various diseases [1,2]. These compounds are effectively used for treatment of different kinds of fungal and bacterial infections as well as non-infectious diseases including gastric ulcer and cancer. Sulfur is forming both σ and π bonds, so research on their binding interactions with receptor [3]. Moieties have also been an interesting field of study during the past decade. Thiazoles are useful structural units in the field of medicinal chemistry and they have shown a wide variety of biological effectiveness [4]. The thiazole nucleus is present in the structure of many natural and biologically active substances, such as vitamin-B and some drugs like penicillins, cephalosporins [5], Abafungin, Famotidine, Meloxicam, Pramipexole, Riluzole, Sudoxicam, Sulfathiazole, Talipexole [6]. Several reports showed Thiazole containing $\text{N}=\text{C}=\text{S}$ moiety's effectiveness as antibacterial, antifungal [7], anti-inflammatory [8], analgesic [9], antitubercular [10], antipsychotics and antimalarial [11], as well as central nervous system (CNS) stimulant [12] anti-HIV [13] etc. Thiazide derivatives are introduced as useful clinical agents and some of its derivatives are inhibitors of herpes simplex viruses [14]. Herein, we report a hitherto, three-component reaction, green synthesis which, starting from readily available benzoyl isothiocyanate, secondary amines, and acetylenedicarboxylates, afforded the alkyl 2-(dialkylamino)-4-phenylthiazole-5-carboxylates (6a-6l). All the synthesized compounds were screened for their antibacterial activities against some selected bacteria with determining their Minimum inhibitory and bactericidal concentration values.

EXPERIMENTAL SECTION

Synthesis of compound

Starting materials and solvents were obtained from Merck (Germany) and Fluka (Switzerland) and were used without further purification. Flash chromatography (FC): preparation of columns with Merck silica gel (SiO_2) powder. MP: Electrothermal-9100 apparatus; uncorrected. IR Spectra: Shimadzu-IR-460 spectrometer; δ in cm^{-1} . ^1H - and ^{13}C -NMR Spectra: Bruker-DRX-300-Avancespectrometer; at 300.13 (^1H) and 75.467 MHz (^{13}C); in CDCl_3 ; δ in ppm rel. to Me_4Si as internal standard, J in Hz. MS: Finnigan-MAT-8430 mass spectrometer; ionization potential 20 eves. Elemental analyses: Heroes-CHN-O-Rapid analyzer.

Compounds 6a–6l: General Procedure. To a stirred soln. of benzoyl isothiocyanate 1 (1 moll) and secondary amine 2 (1 moll) in dry CH_2Cl_2 (5 ml) was added drop wise a mixture of daily but-2-yndioate 4 (1 moll) in dry CH_2Cl_2 (3 ml) at r.t. over 2 min. Then, after 0.5 h, SiO_2 powder (2g) was added and the solvent was evaporated. The dry materials were heated for 1 h at 90°C and then placed on top of a column of SiO_2 (10 g). The column was washed with Accost/light petroleum ether 2: 10. The solvent was then evaporated: product 8. The structures of products 6 were confirmed by their IR and ^1H -NMR and ^{13}C -NMR [15].

Bacterial material

The antimicrobial activity was investigated by tube-dilution method by using the Clinical and Laboratory Standards Institute (CLSI) guidelines. This method is based on the inhibitory effect of a uniform solution of antibiotic in a broth culture on a bacterium with defined numbers. In this method minimal inhibitory concentration (MIC) as well as minimal bactericidal concentration (MBC) of the antimicrobial agent was determined. The MIC is the lowest concentration of an antimicrobial agent that inhibits the growth of the test bacterium whereas MBC is the lowest concentration of an antimicrobial agent that kills the bacterium. Antibacterial activity of synthesized compounds were tested against several gram positive and gram negative bacteria including: *Staphylococcus epidermis's* ATCC.14990, *Bacillus subtilis* ATCC.12711, *Pseudomonas aeruginosa* ATCC 27853 *Staphylococcus aureus* ATCC 25923, *Acinetobacter calcoaceticus* ATCC 23055, and *Escherichia coli* ATCC 25922. The MICs and MBCs of the synthesized compounds were determined using sterile glass test tubes containing Muller-Hinton broth (Merck). The inoculum contained 1.5×10^6 cells/ml of each tested bacterium. The synthesized compounds were tested in respect of their antibacterial effects in the range of 0.078 to 2.5 $\mu\text{g/ml}$. compounds were prepared in DMSO and freshly diluted on the day of testing. A tube containing growth medium without any chemicals or antibiotics and Ceftizoxime (in the range of 100-0.975 mg/ml) were used as positive and negative growth controls respectively. Experiments were performed at least three times and the moral values were selected.

RESULTS AND DISCUSSION

The title compounds were prepared within a one-step synthesis which consists in the reaction of *N*-benzoylthiourea derivatives (3), which were derived from the addition of secondary amines (2) to benzoyl isothiocyanate (1), with acetylene dicarboxylates (=but-2-yndioates) (4) proceeded in CH_2Cl_2 at room temperature to give compound (5). SiO_2 Powder was found to catalyze the conversion of (5) to the alkyl 2-(dialkylamino)-4phenylthiazole-5-carboxylates (6) under solvent-free conditions at 90°C in fairly good yields without the formation of by-products (Figure1).

Spectra: The mass spectra of these compounds displayed molecular-ion peaks at the appropriate m/z values. The ^1H -NMR spectrum (CDCl_3) of 6i consisted of a doublet for the two Me_2CH groups (p_h . 1.42, $^3J_{H,H} = 6.9$ Hz), a singlet for the Meow group (p_h . 3.74), a multiplayer for the two Me_2CH groups (p_h . 3.92–3.96), and two multiplayer for the aromatic H-atoms (p_h . 7.39–7.42 and 7.81–7.84). The ^1H -decoupled ^{13}C -NMR spectrum of 6i showed 11 distinct resonances; a partial assignment of these resonances is given in the Exper Part. The ^1H - and ^{13}C -NMR spectra of compounds 6a–6l were similar to those of 6i, except for the resonances of the R, R', Rgroups (Table 1) which exhibited characteristic signals with appropriate chemical shifts (Table 1).

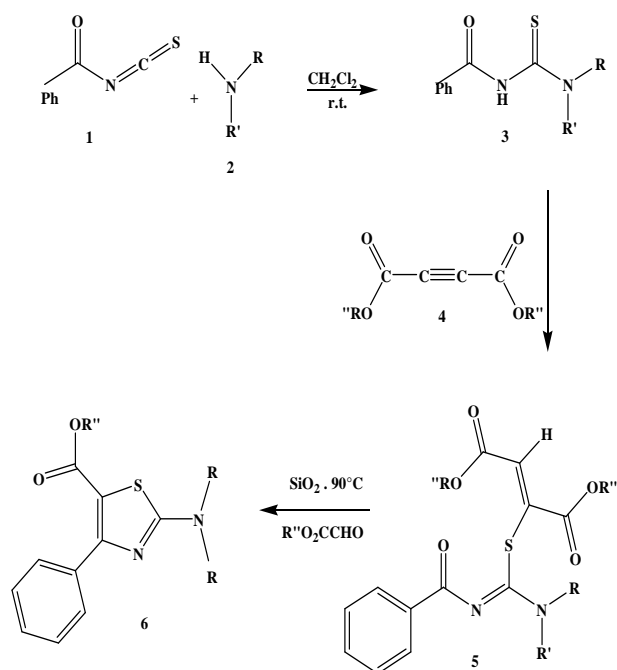


Figure 1. The synthesis scheme employed to obtain the target compounds

Table 1. Synthesis of Alkyl 2-(Dialkylamino)-4-phenylthiazole-5-carboxylates 6

6a-6l

6	R	R'	R''	%Yield
a	-(CH ₂) ₂ -O-(CH ₂) ₂ -		Me	84
b	-(CH ₂) ₂ -O-(CH ₂) ₂ -		Et	80
c	PhCH ₂	Me	Me	80
d	PhCH ₂	Me	Et	77
e		-(CH ₂) ₅ -	Me	81
f		-(CH ₂) ₅ -	Et	79
g	PhCH ₂	PhCH ₂	Me	78
h	PhCH ₂	PhCH ₂	Et	75
i	<i>i</i> -Pr	<i>i</i> -Pr	Me	85
j	<i>i</i> -Pr	<i>i</i> -Pr	Et	83
k	Et	Et	Me	86
l	Et	Et	Et	85

Methyl 2-(Morpholin-4-yl)-4-phenylthiazole-5-carboxylate (6a) :

Yield 255 mg (84%). White crystals. M.p. 130.0°C. IR (KBr): 3065, 2955, 2924, 1735, 1534, 1483, 1237, 1114. ¹H-NMR: 3.59–3.62 (m, (CH₂)₂N); 3.75 (s, Me); 3.82–3.83 (m, (CH₂)₂O); 7.39 (bra, 3arom. H); 7.72 (bra, 2 aroma. H). ¹³C-NMR: 51.74 (Me); 47.99 ((CH₂)₂N); 66.04 ((CH₂)₂O); 127.63, 129.15, 129.76 (5arom. C); 133.48, 135.01, 160.74, 162.74(4C); 170.02 (C=O). EI-MS: 304 (100, M⁺), 285 (6), 273 (20), 259 (18), 247 (70), 231 (13), 215 (28), 201(8), 133 (23), 89 (28), 76 (10). Anal.calc. for C₁₅H₁₆N₂O₃S (304.36): C 59.19, H 5.30, N 9.20; found: C 59.02, H 5.16, N 9.17.

Ethyl 2-(Morpholin-4-yl)-4-phenylthiazole-5-carboxylate (6b):

Yield 254 mg (80%). White crystals. M.p. 90.0–91.0°C. IR (KBr): 3053, 2980, 2924, 1708, 1528, 1482, 1368, 1250. ¹H-NMR: 1.27 (t, ³J_{HH}=7.2 Hz, MeCH₂); 3.59–3.62 (m, (CH₂)₂N); 3.81–3.85 (m, (CH₂)₂O); 4.21 (q, ³J_{HH}=7.2 Hz, MeCH₂); 7.39–7.41 (m, 3arom. H); 7.72–7.74 (m, 2 aroma. H). ¹³C-NMR: 14.21 (MeCH₂); 47.98 ((CH₂)₂N); 60.70 (MeCH₂); 66.05((CH₂)₂O); 127.56, 129.02, 129.78 (5 aroma. H); 133.56, 135.31, 160.85, 162.90 (4 C); 170.41

(C=O). EIMS: 318 (100, M^+), 304 (7), 289 (9), 273 (27), 260 (73), 246 (24), 232 (32), 215 (29), 188 (41), 133 (71), 105 (52), 39 (85), 77 (29), 56 (40). Anal. Calc. for $C_{16}H_{18}N_2O_3S$ (318.39): C 60.36, H 5.70, and N 8.80; found: C 60.27, H 5.61, and N 8.73.

Methyl2-[Methyl(phenylmethyl)amino]-4-phenylthiazole-5-carboxylate (6c): Yield 270 mg (80%). White crystals. M.p. 77.2°C. IR (KBr): 3025, 2984, 2943, 1710, 1604, 1550, 1330, 1244. 1H -NMR: 3.11 (s, MeN); 3.75 (s, MeO); 4.79 (s, CH_2N); 7.33–7.42 (m, 8 arom. H); 7.79–7.80 (m, 2 arom. H). ^{13}C -NMR: 37.88 (MeN); 51.61 (MeO); 55.97 (CH_2N); 127.57, 127.74, 127.86, 128.81, 129.87 (10 arom. C); 129.01, 134.77, 136.01, 160.41, 162.38 (5 C); 170.96 (C=O). EI-MS: 338 (85, M^+), 329 (47), 309 (37), 247 (11), 215 (24), 188 (14), 146 (18), 120 (15), 103 (13), 91 (100), 77 (13), 65 (17). Anal. calc. for $C_{19}H_{18}N_2O_2S$ (338.42): C 67.43, H 5.36, N 8.28; found: C 67.36, H 5.30, N 8.10.

Ethyl2-[Methyl(phenylmethyl)amino]-4-phenylthiazole-5-carboxylate (6d): Yield 271 mg (77%). White crystals. M.p. 73.2°C. IR (KBr): 3059, 2983, 2926, 1702, 1605, 1550, 1331, 1242. 1H -NMR: 1.25 (t, $^3J_{HH}=7.0$ Hz, $MeCH_2$, EtO); 3.10 (s, MeN); 4.211 (q, $^3J_{HH}=7.0$ Hz, $MeCH_2$); 7.32–7.39 (m, 8 arom. H); 7.78–7.79 (m, 2 arom. H). ^{13}C -NMR: 14.29 ($MeCH_2$); 37.89 (MeN); 55.93 (CH_2N); 60.55 ($MeCH_2$); 127.52, 127.73, 127.83, 128.79, 129.90 (10 arom. C); 128.93, 134.89, 136.07, 160.07, 162.17 (5C); 170.90 (C=O). EI-MS: 352 (27, M^+), 327 (13), 323 (14), 279 (8), 215 (10), 167 (26), 149 (86), 104 (100), 91 (58), 70 (54), 57 (34), 43 (48). Anal. calc. for $C_{20}H_{20}N_2O_2S$ (352.45): C 68.16, H 5.72, N 7.95; found: C 68.02, H 5.64, N 7.81.

Methyl 4-Phenyl-2-(piperidin-1-yl)thiazole-5-carboxylate (6e):

Yield 244 mg (81%). White crystals. M.p. 90.7°C. IR (KBr): 3065, 2997, 2962, 2946, 1715, 1531, 1482, 1340, 1303, 1245, 1145. 1H -NMR: 1.67–1.72 (m, 3 CH_2 (piperidin ring)); 3.57–3.59 (m, 2 CH_2 (piperidin ring)); 3.74 (s, Me); 7.39–7.41 (m, 3 arom. H); 7.74–7.77 (m, 2 arom. H). ^{13}C -NMR: 23.99, 25.12, 49.17 (5 CH_2); 51.53 (MeO); 127.54, 128.90, 129.76 (5 arom. C); 130.86, 134.91, 160.38, 162.44 (5C); 170.90 (C=O). EI-MS: 302 (25, M^+), 273 (14), 246 (17), 167 (17), 149 (39), 84 (21), 58 (41), 43 (100). Anal. calc. for $C_{16}H_{18}N_2O_2S$ (302.39): C 63.55, H 6.00, N 9.26; found: C 62.10, H 5.82, N 9.00.

Ethyl 4-Phenyl-2-(piperidin-4-yl)thiazole-5-carboxylate (6f):

Yield 249 mg (79%). Viscous oil. IR (KBr): 3056, 2936, 2855, 1708, 1677, 1532, 1243. 1H -NMR: 1.25 (t, $^3J_{HH}=7.0$ Hz, $MeCH_2$); 1.66–1.71 (m, 3 CH_2 (piperidine ring)); 3.58–3.57 (m, 2 CH_2 (piperidine ring)); 4.20 (q, $^3J_{HH}=7.0$ Hz, $MeCH_2$); 7.38–7.40 (m, 3 arom. H); 7.73–7.76 (m, 2 arom. H). ^{13}C -NMR: 14.25 ($MeCH_2$); 23.76, 25.13, 49.17 (5 CH_2 (piperidine ring)); 60.46 ($MeCH_2$); 127.49, 128.82, 129.79 (5 arom. C); 130.86, 134.10, 159.99, 162.05 (4C); 170.84 (C=O). EI-MS: 318 (60, M^+), 275 (100), 261 (96), 299 (20), 201 (13), 174 (15), 129 (15), 104 (13), 89 (18), 43 (32). Anal. calc. for $C_{17}H_{20}N_2O_2S$ (316.42): C 64.53, H 6.37, N 8.85; found: C 64.26, H 6.21, N 8.73.

Methyl2-[Bis(phenylmethyl)amino]-4-phenylthiazole-5-carboxylate (6g): Yield 322 mg (77%). White crystals. M.p. 107.6°C. IR (KBr): 3061, 32029, 2936, 1677, 1604, 1528, 1310, 1263. 1H -NMR: 3.73 (s, Me); 4.72 (s, 2 CH_2); 7.29–7.40 (m, 12 arom. H); 7.80–7.3 (m, 3 arom. H). ^{13}C -NMR: 51.59 (Me); 53.40 (2 CH_2); 127.55, 127.89, 128.81, 129.94 (15 arom. C); 129.05, 134.68, 135.75, 160.10, 162.31 (6C); 171.12 (C=O). EI-MS: 414 (20, M^+), 323 (82), 291 (8), 149 (4), 133 (7), 105 (6), 91 (100), 65 (12). Anal. calc. for $C_{25}H_{22}N_2O_2S$ (414.52): C 72.44, H 5.35, N 6.76; found: C 68.02, H 5.64, N 7.81.

Ethyl2-[Bis(phenylmethyl)amino]-4-phenylthiazole-5-carboxylate (6h): Yield 321 mg (75%). White crystals. M.p. 73.1°C. IR (KBr): 3060, 3028, 2978, 2912, 1708, 1534, 1481, 1331, 1237. 1H -NMR: 1.25 (t, $^3J_{HH}=7.1$ Hz, $MeCH_2$); 4.21 (q, $^3J_{HH}=7.1$ Hz, $MeCH_2$); 4.73 (s, (CH_2)₂N); 7.27–7.40 (m, 12 arom. H); 7.82–7.83 (m, 3 arom. H). ^{13}C -NMR: 14.28 ($MeCH_2$); 53.32 (CH_2)₂N); 60.57 ($MeCH_2$); 127.50, 127.87, 127.89, 128.80, 129.98 (15 arom. C); 128.97, 134.81, 135.82, 159.78, 161.96 (6 C); 171.10 (C=O). EI-MS: 428 (3, M^+), 337 (7), 279 (4), 206 (8), 191 (15), 167 (20), 149 (66), 105 (91), 91 (73), 70 (98), 59 (97), 48 (100). Anal. calc. for $C_{26}H_{24}N_2O_2S$ (428.55): C 72.87, H 5.64, N 6.54; found: C 72.75, H 5.56, N 6.41.

Methyl2-[Bis(1-methylethyl)amino]-4-phenylthiazole-5-carboxylate (6i): Yield 271 mg (85%). White crystals. M.p. 105.4°C. IR (KBr): 3020, 2965, 2929, 1706, 1600, 1526, 13331, 1258. 1H -NMR: 1.42 (d, $^3J_{HH}=6.9$ Hz, 2 $MeCH_2$); 3.74 (s, MeO); 3.91–3.96 (m, 2 (Me)₂CH); 7.3–7.45 (m, 3 arom. H); 7.81–7.84 (m, 2 arom. H). ^{13}C -NMR: 20.02 (Me_2CH); 51.15 (MeO); 51.44 (2 Me_2CH); 127.38, 128.78, 129.95 (5 arom. C); 130.86, 135.13, 160.05, 162.62 (4C); 168.01 (C=O). EI-MS: 318 (44, M^+), 261 (28), 234 (100), 57 (38), 41 (55). Anal. calc. for $C_{17}H_{22}N_2O_2S$ (318.43): C 64.12, H 6.96, N 8.80; found: C 63.87, H 6.71, N 8.65.

Ethyl2-[Bis(1-methylethyl)amino]-4-phenylthiazole-5-carboxylate (6j): Yield 278 mg (83%). White crystals. M.p. 90.5°C. IR (KBr): 3080, 3047, 2966, 2930, 1700, 1603, 1529, 1260. 1H -NMR: 1.27 (t, $^3J_{HH}=7.1$ Hz, $MeCH_2$);

1.42 (d, $^3J_{\text{HH}}=6.9$ Hz, Me_2CH); 3.91–3.95 (m, 2 Me_2CH); 4.21 (q, $^3J_{\text{HH}}=7.1$ Hz, MeCH_2); 7.38–7.41 (m, 3 arom. H); 7.81–7.84 (m, 2 arom. H). ^{13}C -NMR: 14.34 (MeCH_2); 20.04 ($2\text{Me}_2\text{CH}$); 51.14 (MeCH_2); 60.31 ($2\text{Me}_2\text{CH}$); 127.32, 128.68, 129.99 (5 arom. C); 130.87, 135.28, 159.76, 162.25 (4C); 167.98 (C=O). EIMS: 332 (58M^+), 289 (100), 275 (86), 261 (18), 247 (21), 229 (15), 174 (15), 148 (35), 129 (17), 103 (28), 39 (21), 43 (24). Anal.calc. for $\text{C}_{18}\text{H}_{24}\text{N}_2\text{O}_2\text{S}$ (332.46): C 65.03, H 7.28, N 8.43; found: C 64.21, H 6.46, N 8.01.

Methyl 2-(Diethylamino)-4-phenylthiazole-5-carboxylate (6k): Yield 250 mg (86%). White crystals. M.p. 81.4°C. IR (KBr): 3054, 3025, 2974, 2934, 1710, 1600, 1511, 1481, 1331, 1263. ^1H -NMR: 1.26 (t, $^3J_{\text{HH}}=6.9$ Hz, 2 MeCH_2); 3.54–3.57 (m, 2 MeCH_2); 3.73 (s, MeO); 7.39 (br., 3 arom. H); 7.75 (br., 2 arom. H). ^{13}C -NMR: 12.49 (2 MeCH_2); 45.46 (2 MeCH_2); 51.61 (MeO); 127.51, 128.88, 129.80 (5 arom. C); 133.15, 134.99, 160.56, 162.47 (4 C); 169.45 (C=O). EI-MS: 290 (50, M^+), 275 (12), 261 (39), 247 (77), 229 (15), 215 (23), 201 (13), 149 (21), 133 (32), 103 (28), 89 (39), 57 (42), 42 (100). Anal.calc. for $\text{C}_{15}\text{H}_{18}\text{N}_2\text{O}_2\text{S}$ (290.38): C 62.04, H 6.25, N 9.65; found: C 61.24, H 6.14, N 8.86.

Ethyl 2-(Diethylamino)-4-phenylthiazole-5-carboxylate (6l):

Yield 259 mg (85%). White crystals. M.p. 90.1°C. IR (KBr): 3051, 2975, 2929, 1698, 1551, 1330, 1258. ^1H -NMR: 1.23–1.31 (m, 3 MeCH_2); 3.56 (q, $^3J_{\text{HH}}=7.2$, 2 MeCH_2N); 4.20 (q, $^3J_{\text{HH}}=7.2$ Hz, MeCH_2O); 7.38–7.40 (m, 3 arom. H); 7.75–7.76 (m, 2 arom. H). ^{13}C -NMR: 12.49 (2 MeCH_2N); 14.28 (MeCH_2O); 45.41 (2 MeCH_2N); 60.38 (MeCH_2O); 127.44, 128.77, 129.84 (5 arom. C); 133.44, 135.14, 160.19, 162.10 (4 C); 169.41 (C=O). EI-MS: 304 (100, M^+), 289 (12), 275 (35), 261 (80), 247 (17), 232 (27), 215 (17), 202 (12), 188 (14), 133 (23), 103 (18), 89 (33), 71 (14). Anal. calc. for $\text{C}_{16}\text{H}_{20}\text{N}_2\text{O}_2\text{S}$ (304.41): C 63.13, H 6.62, N 9.20; found: C 63.4, H 6.56, N 8.93.

Table 2. Minimum inhibitory concentrations of synthesized compounds ($\mu\text{g}/\text{mL}$) for tested bacteria

N	<i>S. aureus</i> ATCC25923	<i>S. epidermidis</i> ATCC.14990	MIC($\mu\text{g}/\text{mL}$) <i>P. aeruginosa</i> ATCC.27853	<i>A. calcoaceticus</i> ATCC 1318	<i>E. coli</i> ATCC.25922	<i>B. subtilis</i> ATCC.12711
1	7	250	500	500	62.5	7.8
2	7	250	250	500	500	62.5
3	7	125	250	250	15.6	31.25
4	7	500	250	1000	250	1.95
5	3.9	15	250	1000	500	0.097
6	3.9	15	250	1000	500	62.5
7	3.9	7	500	1000	250	15.62
8	3.9	7	125	500	250	7.81
9	7	125	125	250	250	62.5
10	7	125	250	250	250	62.5
11	7	7	250	250	250	7.81
12	7	125	250	250	500	62.5
Ceftizoxime	3.9	3.9	3.9	7	62.5	0.0485

Table 3. Minimum bactericidal concentrations of synthesized compounds ($\mu\text{g}/\text{mL}$) for tested bacteria

N	<i>S. aureus</i> ATCC25923	<i>S. epidermidis</i> ATCC.14990	MBC($\mu\text{g}/\text{mL}$) <i>P. aeruginosa</i> ATCC.27853	<i>A. calcoaceticus</i> ATCC 1318	<i>E. coli</i> ATCC.25922	<i>B. subtilis</i> ATCC.12711
	15	31	500	1000	62.5	7.8
2	125	250	500	1000	500	62.5
3	62.5	250	250	1000	31	31.25
4	62.5	500	500	1000	500	62.5
5	62.5	500	250	1000	500	0.097
6	62.5	250	250	1000	1000	62.5
7	62.5	31	500	1000	500	15.62
8	62.5	31	250	1000	500	7.81
9	62.5	125	250	500	500	62.5
10	62.5	125	250	250	500	62.5
11	31.25	125	250	250	500	7.81
12	62.5	125	250	250	500	62.5
Ceftizoxim	31.25	31	3.9	31	62.5	0.0485

Biological results

The antibacterial effects of compounds were compared with ceftizoxime as a reference. As can be deduced from tables, most of the synthesized compounds exhibited noticeable antibacterial activity against gram-positive bacteria including *Staphylococcus epidermidis*, *Bacillus subtilis* and *Staphylococcus aureus*. The results depicted in tables 1 and 2 revealed that compounds 6e, 6f, 6g and 6h showed comparable activity with ceftizoxime against tested Gram-positive bacteria. Also compounds 6a and 6c displayed significant activity against *Escherichia coli*. The MICs and

MBCs of the synthesized compounds, against various selected Gram-positive and Gram-negative bacteria are shown in Tables 2 and 3 respectively.

The new 2-aminothiazol derivatives with piperidin and Bisphenylmethyl moiety exhibited a fairly broad spectrum antimicrobial activity against Gram-positive microorganisms. The aromatic compounds will improve the lipophilic nature of the compound at the same time methyl substituted compound would act as an electron donors. In addition the presence of an amine group at the 2nd position of thiazole would be the essential element for hydrogen bonding with receptor.

CONCLUSION

Some of the synthesized compounds exhibited promising antibacterial activity against gram positive bacteria comparable with Ceftriaxone. Furthermore the easy workup, high yield, and short reaction times makes the method a useful addition for preparing modern pharmaceutical synthetics.

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