Synthesis, Characterization and Preliminary Antimicrobial Evaluation with DFT Study of New Thiazole Derivatives
Sumayah S. Abbas* and Ammar A. Mahmood Kubba*.1

Abstract
Two compounds, 2-amino-4-(4-nitrophenyl)1,3-thiazole(4) and 2-amino-4-(4-bromo phenyl)1,3-thiazole(5), were synthesized by refluxing thiourea (1) with each of para- nitrophenacyl bromide (2) and para-bromophanacyl bromides (3) respectively, in dry methanol. Then, by reaction of compound (5) with 3,5-dinitrobenzoyl chloride in dimethylformamide (DMF) yielded compound (6). On the other hand, reaction of compound (4) with chloroaecetyl chloride in dry benzene afforded compound (7), which is upon treatment with thiourea in dry methanol, afforded compound (8). The characterization of the titled compounds were performed utilizing FTIR spectroscopy, 1H NMR, CHNS elemental analysis and by measurements of their physical properties. The synthesized compounds had been screened for their activity against four Gram positive bacteria (Staphylococcus aureus, Micrococcus luteus, Bacillus subtilis and Bacillus pumilus), and four Gram negative bacteria (Pseudomonas aeruginosa, Escherichia coli, Proteus mirabilis and Klebsiella pneumoniae) and three fungi species: (Saccharomyces cerevisiae, Candida Tropicalis and Candida albicans) using a minimum inhibitory concentration (MIC) of 100 µg/ml of a derivative in dimethylsulfoxide, by well diffusion method. Compound (6) showed moderate antibacterial activity against some tested bacteria (Bacillus pumilus and Bacillus Subtilis) and a moderate antifungal activity towards Candida albicans. Computational study was performed to calculate some of the thermodynamic parameters of synthesized derivatives by using density functional theory (DFT).

Keywords: Antimicrobial, Thiazole, DFT

تحضير تشخيص والتمييز الأولي للميكروبات مع دراسة نظرية الكثافة الوظيفية

النحاية
تم تشخيص الميكروبات المحضر بالاستعانة بالطرق التحليلية، والرئتين النووي، المذاب، والتحليل العملي.

المقدمة
تم تجهيز النشاط الأولي المحتمل للميكروبات ضد أربع أنواع من البكتيريا الموجبة للصبغة غرام، وهي: (الميكروبات المعتدلة النهائية، المكروبات المتقدمة، المكروبات الوراثية، وعصورية بوليسين)، وكذلك ضد أربعة أنواع من البكتيريا السالبة للصبغة غرام وهي: (المكروبات الزائفة، المكروبات الزائفة الوراثية، المكروبات الزائفة الوراثية، والبكتيريا السالبة) باستخدام 100 ميكروبرين من المادة مادة في 1 مل من الديميثيل سلكوبين. كافل مركز مختبر كرستال بفضل الكثافة النسبية. أو مختبر الاضطلاع.

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Introduction

Thiazole is a five membered aromatic heterocyclic ring containing sulfur and nitrogen in its structure. Thiazole derivatives have received a great attention due to their remarkable reported different biological activities such as inhibitors of neuronal nitric oxide synthase\(^1\), anti-cancer \(^2\), antimicrobial \(^3-9\), calcium-activated small conductance potassium channel blockers\(^10\), antilucregenic\(^11\), adenosine A3 receptor antagonists \(^12\), antitumor \(^13\), antifungal \(^14\) and anti-inflammatory activities\(^15-16\).

The thiazole ring moiety is an integral part of many potent biologically active pharmaceutical products such as pramipexole (dopamine agonist indicated for treating Parkinson's disease) \(^17\), mecloxam (NSAID drug, COX-2 inhibitor) \(^18\) and in many third generation cephalosporins \(^19\). Thiazole ring is also found naturally in the essential vitamin B\(_1\) thiamin \(^20\). DFT calculations were used to study the quantitative structure-activity relationships (QSAR).

Materials and Methods

All chemicals and solvents used during synthesis were of analytical grade and used without further purification. Completion of reactions and the purity of compounds were ascertained by thin-layer chromatography (TLC), using Silica gel GF\(_254\) (type 60) precoated aluminium sheets, Merck (Germany) exposed to UV-254nm light and the eluant used is ethyl acetate: n-hexane 4:6 for compounds (4), (7) and (8), and ethyl acetate: n-hexane 5:5 for compounds (5) and (6) to run TLC. Melting points were determined using Stuart SMP3 melting point apparatus in open capillary tubes, and are uncorrected. Fourier-Transform Infrared spectroscopy (FTIR), (KBr disc) (u, cm\(^{-1}\)) were recorded using (Biotech engineering management FTIR-600, UK) at the University of Baghdad /College of Education for Pure Sciences Ibn Al-Haitham /central service laboratory.

Furthermore, the elemental microanalysis of the synthesized compounds was done using (Elemental vario MICRO cube instrument, Germany) in the University of Mustansiriya-College of Pharmacy. \(^1\)HNMR spectra were recorded on BRUKER model Ultra shield 300 MHz spectrophotometer with tetramethylsilane (TMS) as an internal standard, chemical shift were expressed as (\(\delta\)-ppm) and coupling constant in (Hz), and it was run in Al al-Bayt University, Amman, Jordan. The synthetic method is depicted in scheme 1.

Chemical synthesis

General method for synthesis of parent nucleus (4and 5)\(^21\)

A mixture of thiourea (1) (0.01 mol, 0.76g) and each of: 4-nitro phenacyl bromide (2) (0.005 mol, 1.22 g) or of 4-bromo phenacyl bromide (3), (0.005 mol,1.38 g) were dissolved in 100 ml of dry methanol in a round bottom flask and refluxed for 3-4 h. After completion of reaction, as monitored using TLC, the mixture was cooled to room temperature then poured into cold water. The solid separated was collected by filtration. The residue obtained was dried, recrystallized from absolute ethanol.

2-amo-4-(4-nitro phenyl thiazole) (4)

Orange powder; yield 80%; m.p. 288-291°C; \(\textbf{IR} \ (\text{KBr},(u, cm^{-1}) \ : \ 3398 \text{ and } 3282 \text{ cm}^{-1} \ prim. \ (\text{NH} \text{H}) \text{ str.} ; \ 3113 \text{ cm}^{-1} \text{ prim. (N\text{H}) str.} ; 3153 \text{ cm}^{-1} \text{ Ar-(C-H) str.} ; 1641 \text{ cm}^{-1} \text{ (C-N) str.} ,1593\&1325 \text{ cm}^{-1} \text{ asy. and sym. (N=O) str.} ,1539 \text{ cm}^{-1} \text{ (N=O) str.} ,1207 \text{ cm}^{-1} \text{ (C-N) str,1038 & 845 cm}^{-1} \text{ in plane & out of plane} \text{ Ar(C-H) str.} ,717 \text{ cm}^{-1} \text{ out of plane} \text{ Ar-(C=C) str,663cm}^{-1} \text{ (C=S) str.}

2-amino-4-(4-bromo phenyl thiazole) (5)

Off white to pink powder; yield 73%; m.p. 181-184°C ; \(\textbf{IR} \ (\text{KBr},(u, cm^{-1}) \ : \ 3429 \text{ and } 3282 \text{ cm}^{-1} \ prim. \ (\text{NH} \text{H}) \text{ str.} ; 3113 \text{ cm}^{-1} \text{ Ar-(C-H) str.} ,1633 \text{ cm}^{-1} \text{ (C-N) str } ,1533 \text{ cm}^{-1} \text{ (N-H) str.} ; 1473 \text{ cm}^{-1} \text{ Ar(C=C) str,} ,1198 \text{ cm}^{-1} \text{ (C-N) str.} , 1038 & 906 \text{ cm}^{-1} \text{ in plane & out of plane} \text{ Ar(C-H) str.} , 727 \text{ cm}^{-1} \text{ out of plane} \text{ Ar(C=C) str.} , 669 \text{ (C=Br) str.} , 636 \text{ cm}^{-1} \text{ (C=S) str.}

General method for synthesis of (6)\(^22\)

3,5-dinitrobenzoyl chloride (0.00078 mol,0.179 g) was added drop-wise to a stirring solution of compound (5) ,0.00078 mol,0.2g) in dimethyl formamide (DMF). The mixture then refluxed for 4 h after completion of reaction as monitored by TLC. The mixture was poured into distilled water to produce a precipitate which was collected by filtration. The residue was neutralized with 5% NaHCO\(_3\) to pH7, and subsequently washed with water. Column chromatography was run using silica gel (60-120 mesh) and the mobile phase used; ethyl acetate: n-hexane (5:5) and recrystallized from aqueous methanol

\(\text{N-(4-(4-bromo phenyl)thiazol-2-yl)-3,5-dinitrobenzamide (6)}\)

Light gray powder; yield 40%; m.p.165-168°C ; \(\textbf{IR} \ (\text{KBr},(u, cm^{-1})\) : 3410 cm\(^{-1}\) sec. amide (N-H str., 3066 cm\(^{-1}\) Ar(C-H) str,1682 cm\(^{-1}\) (C=O) amide str, 1630 cm\(^{-1}\) (C=N) str,1572 cm\(^{-1}\) (N-H) amide amide,, 1539&1346 cm\(^{-1}\) asy. &sym. (N=O)str, 1475cm\(^{-1}\) Ar=C=C)
str. 1319 cm⁻¹ (N=O) bend. 1288 & 908 cm⁻¹ in plane & out of plane Ar(C-H) bend, 1070 cm⁻¹ (C-N) str. 729 cm⁻¹ out of plane Ar(C=C) bend. 675 cm⁻¹ for (C-S) str. 561 cm⁻¹ for (C-Br) str.; ¹HNMR (300 MHz, acetone-d₆, δ= ppm): 11.25 (1H, s, NHCO); 9.15 (2H, s, Ar-H); 8.65 (1H, s, Ar-H); 7.80 (2H, d, Br-2Ar-H); 7.71 (2H, d, Br-2Ar-H); 6.54 (1H, s, H-thiazole(THZ)); CHNS elemental microanalysis Calc., for (C₁₀H₉BrN₂O₅S) Found: C% 42.63, H% 2.13, N% 12.09, S% 7.09; Calc., C% 42.78, H% 2.02, N% 12.47, S% 7.14. General method for synthesis of (7) Synthetic, in dry benzene (30 ml) was cooled from 0-5°C in an ice bath. Chloroacetyl chloride (0.01 mol, 0.79 ml) dissolved in dry benzene (20 ml) was slowly added to the solution with vigorous stirring. When the addition was complete, the reaction mixture was stirred at room temperature for 30 min., then refluxed in a round bottom flask and a reflux condenser for 3 h. The reaction was monitored using TLC, and by using litmus paper which turns red indicative of HCl liberation. Then benzene was removed in rotary evaporator. The residue was neutralized with 5% NaHCO₃ to pH 7, and subsequently washed with water. The product was dried and recrystallized from methanol. 2-chloro-N-(4-(4-nitrophenyl)thiazol-2-yl)acetamide (7) Bright Yellow powder; yield 82%; m.p. 214-217 °C; IR(KBr), ν cm⁻¹: 3354 cm⁻¹ sec. amide (N-H) str. 3105 cm⁻¹ Ar(C-H) str. 3001 & 2947 cm⁻¹ for asym. & sym. aliphatic (CH₂) str. 1701 cm⁻¹ (C=O) amide str., 1597 & 1444 cm⁻¹ asym. & sym. (N=O) str., 1549 cm⁻¹ (N-H) amide bend-, 1504 cm⁻¹ Ar(C=C) str., 1396 cm⁻¹ (CH₃) bend-, 1331 cm⁻¹ (N=O) bend, 1151 cm⁻¹ (C-N) str., 1111 & 849 cm⁻¹ in plane & out of plane Ar(C-H) bend., 849 cm⁻¹ (C=C) str. 737 cm⁻¹ out of plane Ar(C=C) bend., 634 cm⁻¹ for (C-S) str.; ¹HNMR (300 MHz, DMSO-d₆, δ= ppm): 12.76 (1H, s, NHCO); 8.31 (2H, d, NO₂-2Ar-H); 8.16 (2H, d, NO₂-2Ar-H); 8.06 (1H, s, H-THZ); 4.43 (2H, s, CH₂); CHNS elemental microanalysis Calc., for (C₁₂H₁₁N₂O₃S₂) Found: C% 44.66, H% 2.853, N% 14.13, S% 10.428; Calc., C% 44.38, H% 2.71, N% 14.11, S% 10.77. General method for synthesis of (8) (24) Equimolar amount of compound (7) (0.00117 mol, 0.35g) and thiourea (0.00117 mol, 0.089g) in dry methanol was refluxed for 12 h. The solvent was removed in rotary evaporator. The residue was neutralized with 5% NaHCO₃ to pH 7, and subsequently washed with water, filtered and dried. Column chromatography was run using silica gel (60-120 mesh) and the mobile phase used: ethyl acetate: n-hexane (4:6) to purify the titled compound, then recrystallized from aqueous methanol. N-(4-(4-nitrophenyl)thiazol-2-yl)-2-thioureaacetamide (8) Light orange powder; yield 51%; m.p. 260°C (decomposed); IR(KBr), ν cm⁻¹: 3398 & 3303 cm⁻¹ prim. (NH₂) str., 3141 cm⁻¹ sec. amide (N-H) str., 3116 cm⁻¹ Ar(C-H) str., 2981 & 2927 cm⁻¹ asym. & sym. aliphatic (CH₃) str., 1641 cm⁻¹ (C=O) amide str., 1593 cm⁻¹ (N-H) amide bend, 1537 & 1325 cm⁻¹ asym. & sym. (N=O) str. of (NO₂), 1502 cm⁻¹ (C≡N) str. overlapped with Ar(C≡C) str. 1038 cm⁻¹ (C-N) str.; ¹HNMR (300 MHz, DMSO-d₆, δ= ppm): 7.60 (1H, br, NHCO); 8.31 (2H, d, 2Ar-H); 8.04 (2H, d, 2Ar-H); 7.82 (2H, s, NH₂); 7.25 (1H, s, H-THZ); 4.45 (2H, s, CH₂); CHNS elemental microanalysis Calc., for (C₁₂H₁₁N₂O₃S₂) Found: C% 42.30, H% 3.250, N% 20.570, S% 19.684; Calc., C% 42.72, H% 3.29, N% 20.76, S% 19.01.

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Antimicrobial Screening
The antimicrobial activities of the synthesized derivatives were measured using well diffusion technique (25) with a comparison to cefotaxime sodium (cefot.) and sulfamethoxazole (sulf.) as standard antibacterial agents, and miconazole as standard antifungal agent, using dimethylsulfoxide (DMSO) as solvent and as a control, and it was run in the ministry of health / National Center for Drug Control and Research (NCDCR) /Baghdad and in University of Baghdad /College of Education for Pure Sciences Ibn Al-Haitham /central service laboratory. The synthesized compounds had been screened for their in vitro preliminary antimicrobial activity against four Gram positive bacteria (Staph.aureus, Micrococcus luteus, Bacillus subtilis and Bacillus pumilus), four Gram negative bacteria (Pseud.aeruginosa, E.coli, Proteus mirabilis and Klebsiella pneumoniae) and three fungi (Saccharomyces cerevisiae, Candida tropicalis and Candida albicans), using a minimum inhibitory concentration (MIC) of 100 µg/ml of compound in DMSO as shown in tables 1 and 2.

Results and Discussion
Chemistry
The synthesis of parent nucleus (4) and (5), was carried out according to Hantzsch method, by refluxing thiourea (1) and 4-substituted phenacyl bromide (2, R=NO2; 3, R=Br) with methanol Reflux 3 h. Then (4), R=NO2 (5), R=Br and 3,5-dinitrobenzoyl chloride reflux 4 h in DMF. Additionally, (6), R=Br and (7), R=NO2 were reflux 12 h in methanol. Finally, thiourea (1) and 4-substituted phenacyl bromide (2, R=NO2; 3, R=Br) were refluxed in methanol.

Scheme 1. Synthesis of titled thiazole derivatives.
substituted(4-Bromo or 4-nitro) phenacyl bromides \((2)\)and \((3)\) in absolute methanol for 3 hours. They are characterized by FTIR, due to appearance primary amine \((\text{NH}_2)\) stretching at \(3398\) \& \(3305\) cm\(^{-1}\) for compound \((4)\) and \(3429\&3282\) cm\(^{-1}\) for compound \((5)\). Compound \((6)\) characterized by carbonyl amide \((\text{C}=\text{O})\) stretching at \(1682\) cm\(^{-1}\).While \(^1\text{HNMR}\) displayed \((\text{NHCO})\) peak as singlet at \(\delta=11.25\) ppm, and the aromatic ring integrated for seven protons are displayed at their expected region \((\text{see exp. part})\). Compound \((7)\) characterized by the appearance of \((\text{C}=\text{O})\) amide stretching at \(1701\) cm\(^{-1}\) and a characteristic peak, as a singlet due to \((\text{NHCO})\) \(\delta=12.76\) ppm in addition to the aromatic protons displayed at their expected region.

Compound \((8)\) recorded in the IR spectrum two characteristic absorption bands of primary amine (side chain), \((\text{NH}_2)\) stretching, at \(3398\) and \(3303\) cm\(^{-1}\), while \(^1\text{HNMR}\) spectrum displayed a broad peak at \(\delta=12.80\) ppm., attributed to \(\text{NHCO}\), also prominent peak at \(\delta=7.40\) ppm as a singlet due to \(\text{NH}_2\) of thiourea.

It must be noted that the H5-THZ recorded for the compound \((7)\) and \((8)\) as a singlet peak at \(\delta= 8.06\) and \(7.25\) ppm, respectively.

**Antimicrobial activity**

From the data illustrated in tables 1 and 2. Compound \((6)\) showed moderate antibacterial activity against some tested Gram positive bacteria (\(\text{Bacillus pumilus}\) and \(\text{Bacillus subtilis}\)), while compound \((8)\) displayed no antimicrobial effect. In addition, compound \((6)\) displayed moderate antifungal activity against \(\text{Candida albicans}\).

### Table 1. Antimicrobial activity of the tested compounds.

<table>
<thead>
<tr>
<th>Cpd. No.</th>
<th>Conc. µg/ml</th>
<th>Staph. aureus</th>
<th>Micrococcus luteus</th>
<th>Bacillus pumilus</th>
<th>Bacillus subtilis</th>
<th>Pseud. aeruginosa</th>
<th>E.coli</th>
<th>Proteus mirabilis</th>
<th>Klebsiella pneumoniae</th>
</tr>
</thead>
<tbody>
<tr>
<td>(6)</td>
<td>100</td>
<td>-</td>
<td>-</td>
<td>11.3</td>
<td>12</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>(8)</td>
<td>100</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Cefot.</td>
<td>100</td>
<td>50.11</td>
<td>59</td>
<td>41.5</td>
<td>45</td>
<td>32.5</td>
<td>53.2</td>
<td>27</td>
<td>28</td>
</tr>
<tr>
<td>Sulf.</td>
<td>100</td>
<td>24</td>
<td>29</td>
<td>32.4</td>
<td>20</td>
<td>25</td>
<td>27.8</td>
<td>27</td>
<td>23</td>
</tr>
<tr>
<td>DMSO</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

**Notes:** Zone of inhibition (mm)

### Table 2. Antifungal activity of the tested compounds.

<table>
<thead>
<tr>
<th>Compound no.</th>
<th>Conc. µg/ml</th>
<th>Saccharomyces cerevisiae</th>
<th>Candida tropicalis</th>
<th>Candida albicans</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Zone of inhibition(mm)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(6)</td>
<td>100</td>
<td>-</td>
<td>-</td>
<td>10.8</td>
</tr>
<tr>
<td>(8)</td>
<td>100</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Miconazole</td>
<td>100</td>
<td>36.5</td>
<td>16</td>
<td>23.8</td>
</tr>
<tr>
<td>DMSO</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

\((\text{--})=\) No activity, slightly active (Inhibition Zone in between 5-10 mm), moderately active (Inhibition Zone in between 10-15 mm), highly active (Inhibition Zone More Than 15 mm). \((26-28)\)

**Computational Studies**

**Density function theory (DFT)**

In order to explore the theoretical-experimental consistency, quantum chemical calculations were performed with complete geometry optimizations using standard Spartan 10 software. Geometry optimization was carried out by B3LYP / 6-31G* level of theory.

The highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO) play an important role in the molecule. These orbitals are sometimes referred to as the frontier molecular orbital.

Fig.1 shows the frontier molecule orbital density distributions of the investigated compounds. The HOMO orbital is an electron donor and the LUMO orbital is the electron acceptor. The difference in energy between
HOMO orbital and LUMO orbital (energy gap) is a very effective property for characterizing the kinetic stability and chemical reactivity of the molecules. A molecule with a small LUMO-HOMO energy gap is chemically more reactive and kinetically less stable. On the contrary, a large LUMO -

HOMO energy gap corresponds to high kinetic stability and low chemical reactivity (29).

**Structural and electronic properties**

DFT calculations were performed for compounds (2 - 8). Optimized molecular structures of the most stable form are shown in Figure 1.

![Figure 1](image-url)
Synthesis and DFT study of new thiazole derivatives

Compound (5)

HOMO

LUMO

Compound (6)

HOMO

LUMO

Compound (7)

HOMO

LUMO
Compound (8)

Figure 1. Highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO) for compounds (2–8).

As shown in Table 3, the result of theoretical calculations reveals, that in the case of the compounds (2-8), the energy of highest occupied molecular orbital (EHOMO) are -10.804, -10.749, -8.339, -8.086, -2.264, -1.062 and -8.038 eV and the energy of the LUMO orbital (ELUMO) are -7.084, -4.120, -2.943, -1.227, 1.93, 0.474 and -4.826. Thus, the frontier orbital gap are about 3.72, 6.629, 5.396, 6.859, 4.194, 1.536 and 3.212 eV in the compounds (2-8), respectively. As a result, the compound with less energy gap has more kinetic stability and less chemical reactivity than others, like compound (7), whereas the compound with more energy gap has less kinetic stability and more chemical reactivity than others, for example, compound (3).

The linkage between the molecular structures of compounds with its respective biological activities is central to the QSAR paradigm. Molecular descriptors play a crucial role in providing numerical description of the physicochemical properties of molecules. In order to properly account for these structural features, it is essential that suitable descriptors be chosen for QSAR investigation. Electronegativity ($\mu$) essentially provides a measure of the asymmetric distribution of charges in a molecule (29). It can be seen that compounds with the highest electronegativity were compound $2 > 3 > 8 > 4 > 5 > 7 > 6$ with values. It was observed that compound (2). Such high value 8.944 is associated with the asymmetric distribution of electrons as afforded by the strong electron withdrawing nature of compound (2).

log $p$ provides a measure of a molecule’s lipophilicity where high log $p$ value indicates high lipophilicity, while low value suggests low lipophilicity. The results indicated that compounds having the highest lipophilicity were $5 > 3 > 2$ with corresponding values of 3.51, 2.82 and 1.73, respectively. The compound (5), set of a molecule possessed the highest lipophilicity. It can be observed that the energy gaps between HOMO and LUMO of compounds (2-8) is $5 > 3 > 4 > 6 > 2 > 8 > 7$. The larger the HOMO–LUMO energy gap, the harder and more stable/less reactive the molecule, for example, compounds (4), (5) and (8).

Electrostatic potential charges and related quantum chemical properties

The distribution of the electronic density (electrostatic potential charges), related quantum chemical parameters. The highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO) play an important role in the molecule. HOMO/LUMO gap (Table 3, row 4) and the partition coefficients of the compounds (log $p$; Table 3, row 6) were calculated for observed compounds.

Table 3. HOMO and LUMO, and electronic properties units for compounds (2-8) using DFT with B3LYP/6-31G* basis set.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Compound (2)</th>
<th>Compound (3)</th>
<th>Compound (4)</th>
<th>Compound (5)</th>
<th>Compound (6)</th>
<th>Compound (7)</th>
<th>Compound (8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Energy kcal/mol</td>
<td>17.084</td>
<td>14.3827</td>
<td>5.9258</td>
<td>5.9262</td>
<td>10.6845</td>
<td>-3.3102</td>
<td>-2.9732</td>
</tr>
<tr>
<td>LUMO eV</td>
<td>-7.084</td>
<td>-4.120</td>
<td>-2.943</td>
<td>-1.227</td>
<td>1.93</td>
<td>0.474</td>
<td>-4.826</td>
</tr>
<tr>
<td>Energy gap eV</td>
<td>3.72</td>
<td>6.629</td>
<td>5.396</td>
<td>6.859</td>
<td>4.194</td>
<td>1.536</td>
<td>3.212</td>
</tr>
<tr>
<td>Electronegativity ($\mu$)</td>
<td>8.944</td>
<td>7.435</td>
<td>5.641</td>
<td>4.657</td>
<td>0.132</td>
<td>0.294</td>
<td>6.432</td>
</tr>
<tr>
<td>Log P</td>
<td>1.73</td>
<td>2.82</td>
<td>-</td>
<td>3.51</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>
Conclusion
In the present work new derivatives were synthesized starting from 2-amino-4-(4-(nitrophenyl) 1,3-thiazole), and (4) and 2-amino-4-(4-bromophenyl) 1,3-thiazole, using conventional method, the titled derivatives (6) and (8) were evaluated for their preliminary antimicrobial activity using well diffusion method. Compound (6) exhibited moderate antibacterial and antifungal activity against some Gram-positive bacteria (Bacillus pumilus), and Bacillus subtilis and one fungal species (Candida albicans).

The titled thiazole derivatives were studied theoretically by using DFT calculations. the quantum chemistry calculations using the Density Function Theory. (DFT) method of biologically active molecules and can be used for a building of quantitative structure-activity relationship (QSAR) model in the future. Both experimental techniques and theoretical methods were used to determine the structural and spectroscopic properties of compound were in good result of each other.

Acknowledgement
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References