New Thiourea-, and Azomethine Derivatives of 4-Amino-5-[Hydroxy (Diphenyl)Methyl]-2,4-Dihydro-3H-1,2,4-Triazol-3-Thion with Potential Antimicrobial Activity

4-Amino-5-[Hidroksi(Difenil)Metil]-2,4-Dihidro-3H-1,2,4-Triazol-3-Tiyon Yapısından Elde Edilen Bazı Yeni Tiyüre ve Azometin Türevleri ve Antimikrobiyel Aktivitelerinin İncelenmesi

Eser İlhan¹ and Gülten Ötük²

Istanbul University, Faculty of Pharmacy, ¹Department of Pharmaceutical Chemistry, ²Department of Pharmaceutical Microbiology, 34452 Beyazıt - Istanbul, Turkey.

Abstract

New 5-[hydroxy(diphenyl)methyl]-4-[(substituted phenyl)methylidene](amino)-2,4-dihydro-3H-1,2,4-triazol-3-thione, N-(substituted phenyl)-N’-(3-[hydroxy(diphenyl)methyl]-5-thioxo -1,5-dihydro-4H-1,2,4-triazol-4-yl)thiourea and [1,2,4]triazolo[3,4-b][1,3,4] thiadiazole derivatives were synthesized from 4-amino-5-[hydroxy(diphenyl)methyl] -2,4-dihydro-3H-1,2,4-triazol-3-thione. The structures of the new compounds were determined on the basis of analytical (C,H,N) and spectroscopic data (IR, ¹H-NMR , MS ). All the compounds were evaluated for antimicrobial activity against Escherichia coli ATCC 8739, Klebsiella pneumoniae ATCC 4352, Pseudomonas aeruginosa ATCC 1539, Candida albicans ATCC 10231, Staphylococcus aureus ATCC 6538 and Staphylococcus epidermidis ATCC 12228. Some of the compounds were found active against S.aureus and S.epidermidis (MIC 31.2-7.8mcg /ml ).

Key words: 1,2,4-Triazole-3-thione, thiourea, [1,2,4]triazolo[3,4-b][1,3,4]thiadiazole, Antimicrobial activity.

Introduction

The prevalence of resistance and cross resistance against existing chemotherapeutic agents makes antimicrobial research increasingly attractive and stimulates the search for new compounds.

The 1,2,4-triazole nucleus and fused heterocyclic systems derived from it have been reported to demonstrate a wide spectrum of activities (Reid et al.,1976 ; Karow,1981 ;Hassan et al., 1983,Eweiss et al., 1986; Chaturvedi et al., 1988; Habib et al., 1997; Gülerman et al., 1997; Zitouni et al., 1999 ). Besides 1,2,4-triazoles, thiourea derivatives have been reported to exhibit antimicrobial activity (Rollas et al., 1991 ; Küçükgüzel et al., 2001)

* Corresponding author

This work was supported by Istanbul University Resarch Found Project Number Ö – 341 / 200897 .
Prompted by these reports and in continuation of our previous work on the synthesis of heterocycles of pharmaceutical interest, we selected 4-amino-5-[hydroxy(diphenyl)methyl]-2,4-dihydro-3H-1,2,4-triazol-3-thione 2, a versatile substrate for mono and difunctional electrophiles by virtue of its vicinal amino and thione groups as the key intermediate and prepared new derivatives which may exhibit antimicrobial activity. Thus treatment of benzilic acid hydrazide in ethanolic potassium hydroxide with carbon disulfide afforded the potassium salt of 2-[hydroxy(diphenyl)acethyl]hydrazincarbodiithioc acid 1 almost quantitatively (Ergenç et al., 1996). 1 was reacted with hydrazine hydrate according to Reid and Heindel to obtain 2, which was in turn condensed with aromatic aldehydes (Misra et al., 1988) to give the azomethine derivatives 3a–e.

Reaction of 2 in dry dimethylformamide with appropriate isothiocyanates at room temperature (Chaturvedi et al., 1988) yielded new thiourea derivatives 4a–e. The same reaction was also carried out at an elevated temperature to achieve 5, a new triazolo[3,4-b][1,3,4]thiadiazole derivative, according to a literature method (Misra et al., 1988).

The synthetic routes to 1-5 are outlined in scheme 1. The structures of the synthesized compounds were confirmed by elemental analyses (C H N) and spectral data (IR, 1H-NMR, EIMS / CIMS). The molecular formulas, melting points, yields and analytical data of 1-5 are presented in the table.

**Scheme 1**

<table>
<thead>
<tr>
<th>R</th>
<th>3a</th>
<th>R</th>
<th>4a</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cl (2,6)</td>
<td>3a</td>
<td>CeH5</td>
<td>4a</td>
</tr>
<tr>
<td>OCH3 (3,4)</td>
<td>3b</td>
<td>CeH4Br (4)</td>
<td>4b</td>
</tr>
<tr>
<td>NO2 (2,4)</td>
<td>3c</td>
<td>CeH4NO2 (3)</td>
<td>4c</td>
</tr>
<tr>
<td>NO2 (3)</td>
<td>3d</td>
<td>CeH4Cl (3)</td>
<td>4d</td>
</tr>
<tr>
<td>F (4)</td>
<td>3e</td>
<td>CeH4(CH3) (4)</td>
<td>4e</td>
</tr>
</tbody>
</table>
Scheme 1

Table

<table>
<thead>
<tr>
<th>Compd.</th>
<th>Formula</th>
<th>Mp.</th>
<th>Yield</th>
<th>Analysis</th>
<th>C</th>
<th>H</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>( M.W.)</td>
<td>(°C)</td>
<td>(%)</td>
<td>(cald./found)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>C₁₂H₁₂KN₂O₂S₂</td>
<td>245</td>
<td>98.8</td>
<td>50.54/50.60</td>
<td>3.68/3.77</td>
<td>7.86/7.78</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>C₁₅H₁₄N₂O₃</td>
<td>220</td>
<td>76.5</td>
<td>60.38/59.90</td>
<td>4.73/4.70</td>
<td>18.78/18.60</td>
<td></td>
</tr>
<tr>
<td>3a</td>
<td>C₂₂H₁₆Cl₂N₂O₃S</td>
<td>230</td>
<td>80</td>
<td>58.03/57.80</td>
<td>3.54/3.32</td>
<td>12.30/12.73</td>
<td></td>
</tr>
<tr>
<td>3b</td>
<td>C₂₄H₂₂N₂O₃S</td>
<td>235</td>
<td>71</td>
<td>64.56/64.01</td>
<td>4.97/5.20</td>
<td>12.55/12.51</td>
<td></td>
</tr>
<tr>
<td>3c</td>
<td>C₂₂H₁₆N₂O₃S</td>
<td>240</td>
<td>64</td>
<td>55.46/56.17</td>
<td>3.38/3.63</td>
<td>17.64/17.56</td>
<td></td>
</tr>
<tr>
<td>3d</td>
<td>C₂₂H₁₇N₂O₃S</td>
<td>207</td>
<td>68</td>
<td>61.24/61.73</td>
<td>3.97/4.30</td>
<td>16.23/16.78</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Formula</td>
<td>3e C&lt;sub&gt;22&lt;/sub&gt;H&lt;sub&gt;17&lt;/sub&gt;FN&lt;sub&gt;4&lt;/sub&gt;OS (404.47)</td>
<td>4a C&lt;sub&gt;22&lt;/sub&gt;H&lt;sub&gt;18&lt;/sub&gt;N&lt;sub&gt;2&lt;/sub&gt;OS&lt;sub&gt;2&lt;/sub&gt; (433.55)</td>
<td>4b C&lt;sub&gt;22&lt;/sub&gt;H&lt;sub&gt;18&lt;/sub&gt;BrN&lt;sub&gt;2&lt;/sub&gt;OS&lt;sub&gt;2&lt;/sub&gt; (512.45)</td>
<td>4c C&lt;sub&gt;22&lt;/sub&gt;H&lt;sub&gt;18&lt;/sub&gt;N&lt;sub&gt;6&lt;/sub&gt;O&lt;sub&gt;3&lt;/sub&gt;S&lt;sub&gt;2&lt;/sub&gt; (478.54)</td>
<td>4d C&lt;sub&gt;22&lt;/sub&gt;H&lt;sub&gt;18&lt;/sub&gt;ClN&lt;sub&gt;4&lt;/sub&gt;OS&lt;sub&gt;2&lt;/sub&gt; (467.97)</td>
<td>4e C&lt;sub&gt;22&lt;/sub&gt;H&lt;sub&gt;21&lt;/sub&gt;N&lt;sub&gt;2&lt;/sub&gt;OS&lt;sub&gt;2&lt;/sub&gt; (447.57)</td>
</tr>
<tr>
<td>---</td>
<td>------------------</td>
<td>-------------------------------------------------</td>
<td>----------------------------------</td>
<td>----------------------------------</td>
<td>----------------------------------</td>
<td>----------------------------------</td>
<td>-----------------------------------</td>
</tr>
<tr>
<td></td>
<td></td>
<td>217 70 65.33 / 65.40 4.24 / 4.23 13.85 / 13.62</td>
<td>187 47 60.95 / 60.56 4.42 / 4.44 16.15 / 16.78</td>
<td>185 42 51.56 / 51.47 3.54 / 3.72 13.67 / 13.70</td>
<td>205 48 55.22 / 55.02 3.79 / 3.89 17.56 / 17.45</td>
<td>205 37 56.46 / 56.99 3.88 / 4.10 14.96 / 15.08</td>
<td>220 35 61.72 / 60.81 4.72 / 4.59 15.64 / 15.49</td>
</tr>
</tbody>
</table>

**Materials and Methods**

Melting points were determined with a Buchi 530 melting point apparatus and are uncorrected. The spectra were recorded on PerkinElmer 1600 FT (IR), Bruker AC 200 (200 MHz, <sup>1</sup>H-NMR) and VG Zab Spec (70 eV, EI/MS) instruments, respectively. CIMS (CH<sub>4</sub>) were provided by Sittingbourne Research Centre (UK). Elemental analyses were performed on a Carlo Erba 1106 elemental analyzer.

**[Hydroxy(diphenyl)acetyl]hydrazinecarbodiithioic acid potassium salt**

1. 0.025 mol. Benzilic acid hydrazide was dissolved in 40 ml anhydrous ethanol containing 2.25 g KOH with constant stirring. To this solution 5 ml CS<sub>2</sub> were added. The yellow colored reaction mixture thus obtained was further agitated for 1h to effect complete solidification. After suction filtration the crude product was washed with dry ether and dried to afford 1 as a water soluble fine yellow powder.

**IR (KBr) v cm<sup>-1</sup>:** 2920 (Ar C-H), 1660 (C=O), 1480, 1420 (C=C), 1028 (C=S). **EI/MS (m/z) (70 eV):** 357 (M<sup>+</sup>) (2), 224 (19), 195 (5), 193 (5), 165 (10), 183 (55), 131 (3), 105 (100), 77 (67), 51 (28), 44 (15).

**4-Amino-5-[hydroxy(diphenyl)methyl]-2,4-dihydro-3H-1,2,4-triazol-3-thione**

2. To 7.12 g of 1 were added 4 ml water and 2 ml hydrazine hydrate and the reaction mixture thus obtained was refluxed until a white precipitate was obtained. The crude product was diluted with water, filtered and recrystallized from ethanol to yield 2 as fine colorless needles.

**IR (KBr) v cm<sup>-1</sup>:** 3440 (OH), 3300, 3150 (NH), 3025 (Ar C-H), 1615, 1500, 1440 (C=N, C=C). **<sup>1</sup>H NMR (DMSO - d<sub>6</sub>) δ ppm:** 5.14 (NH<sub>2</sub>, 2H, s) 6.63 (OH, 1H, s) 7.22-7.55 (Ph, 10H, m), 13.62 (NH, 1H, s). **CIMS (CH<sub>4</sub>) (m/z):** 299 (M<sup>+</sup>) (35), 281 (60), 211 (5), 183 (100), 157 (2), 145 (4).

**General procedure for the synthesis of 3a-e**

To equimolar amounts of 2 and an appropriate aldehyde in EtOH (10 ml), a few drops of concentrated H<sub>2</sub>S<sub>2</sub>O<sub>7</sub> were added and the reaction mixture was heated under reflux on a water bath both for 1 h. The crude product was precipitated by the addition of water and purified by washing with hot ethanol.

**5-[hydroxy(diphenyl)methyl]-4-[(2,6-dichlorophenyl)methylidene]amino]-2,4-dihydro-3H-1,2,4-triazol-3-thione**

3a

**IR (KBr) v cm<sup>-1</sup>:** 3420 (OH), 3200 (NH), 3070, 3020 (Ar C-H), 1600, 1570, 1475 (C=N, C=C), 1035 (C=S). **<sup>1</sup>H NMR (DMSO - d<sub>6</sub>) δ ppm:** 6.57 (OH, 1H, s), 7.24-7.54 (Ph, 13H, m), 10.36 (CH, 1H, s), 14.18 (NH, 1H, s). **EI/MS (m/z) (70 eV):** 455 (M<sup>+</sup>) (0.4), 283 (25.3), 206 (80.72), 205 (18.57), 183 (7.24), 182 (31.8), 173 (14.92), 105 (100), 101 (35.68), 77 (56.94).

**5-[hydroxy(diphenyl)methyl]-4-[(3,4-dimethoxyphenyl)methylidene]amino]-2,4-dihydro-3H-1,2,4-triazol-3-thione**

3b
IR (KBr) v cm⁻¹: 3400 (OH), 3260 (NH), 3060, 3020 (Ar, C-H), 1600, 1580, 1475 (C=N, C=C), 1050 (C=S). ¹H NMR (DMSO-d₆) δ ppm: 6.74 (OH, 1H, s), 6.92-7.33 (Ph, 13H, m), 10.43 (CH, 1H, s), 13.95 (NH, 1H, s). EIMS (m/z) (70 eV): 283 (3.7), 206 (16.63), 183 (6.82), 182 (41.04), 163 (78.15), 105 (100).

5-[(hydroxy(diphenyl)methyl)-4-[[2,4-dinitrophenyl]methylidene]amino]-2,4-dihydro-3H-1,2,4-triazol-3-thione 3c
IR(KBr) v cm⁻¹: 3460 (OH), 3260 (NH), 3080, 3020 (Ar, C-H), 1610, 1560, 1480 (C=N, C=C), 1050 (C=S). ¹H NMR (DMSO-d₆) δ ppm: 6.93 (OH, 1H, s), 7.22-7.45 (Ph, 13H, m), 10.84 (CH, 1H, s), 14.19 (NH, 1H, s). EIMS (m/z) (70 eV): 475 (3.64), 283 (5.85), 206 (16.63), 193 (9.25), 182 (32.21), 165 (10.55), 105 (100), 101 (21.36), 77 (58.29).

5-[(hydroxy(diphenyl)methyl)-4-[[3-nitrophenyl]methylidene]amino]-2,4-dihydro-3H-1,2,4-triazol-3-thione 3d
IR(KBr) v cm⁻¹: 3430 (OH), 3320 (NH), 3080, 3020 (Ar, C-H), 1610, 1560, 1520, 1470 (C=N, C=C), 1048 (C=S). ¹H NMR (DMSO-d₆) δ ppm: 6.93 (OH, 1H, s), 7.23-7.73 (Ph, 14H, m), 9.75 (CH, 1H, s), 14.11 (NH, 1H, s). EIMS (m/z) (70 eV): 281 (14.32), 207 (100), 182 (15.2), 105 (7.9), 77 (12.02).

5-[(hydroxy(diphenyl)methyl)-4-[[4-fluorophenyl]methylidene]amino]-2,4-dihydro-3H-1,2,4-triazol-3-thione 3e
IR(KBr) v cm⁻¹: 3420 (OH), 3320 (NH), 3080, 3020 (Ar, C-H), 1600, 1580, 1490 (C=N, C=C), 1040 (C=S). ¹H NMR (DMSO-d₆) δ ppm: 6.80 (OH, 1H, s), 7.22-7.57 (Ph, 14H, m), 9.32 (CH, 1H, s), 14.02 (NH, 1H, s). CIMS (CH₄) (m/z): 405 (M⁺) (6.6), 387 (10), 266 (50), 183 (20), 122 (100), 105 (6.5).

General procedure for the synthesis of 4a - e
Equimolar amounts of 2 and an appropriate isothiocyanate in dry dimethylformamide were stirred for 1 h at room temperature. The resulting reaction mixture was poured into ice-water, filtered and recrystallized from ethanol/water.

N-Phenyl-N'-{3-[hydroxy(diphenyl)methyl]-5-thioxo-1,5-dihydro-4H-1,2,4-triazol-4-yl}-thiourea 4a
IR (KBr) v cm⁻¹: 3425 (OH), 3290 (NH), 3155 (Ar, CH), 1630, 1593, 1500 (C=N, C=C), 1265 (C=S). ¹H NMR (DMSO-d₆) δ ppm: 6.75 (OH, 1H, s), 7.1-7.3 (Ph, 15H, m), 9.84 (NH, 2H, s), 13.65 (triazole NH, 1H, s). EIMS (m/z) (70 eV): 433 (M⁺) (4), 385 (23), 357 (18), 341 (16), 311 (24), 283 (15), 298 (76), 279 (87), 183 (22), 165 (37), 135 (10), 128 (14), 152 (40), 118 (57), 105 (95), 93 (50), 77 (100), 65 (22), 61 (17), 60 (21), 59 (12).

N-(4-Bromophenyl)-N'-{3-[hydroxy(diphenyl)methyl]-5-thioxo-1,5-dihydro-4H-1,2,4-triazol-4-yl}-thiourea 4b
IR (KBr) v cm⁻¹: 3430 (OH), 3300 (NH), 3120 (Ar, CH), 1610, 1590, 1500 (C=N, C=C), 1260 (C=S). ¹H NMR (DMSO-d₆) δ ppm: 6.75 (OH, 1H, s), 7.25-7.40 (Ph, 14H, m), 9.85 (NH, 2H, s), 13.40 (triazole NH, 1H, s).

N-(4-Nitrophenyl)-N'-{3-[hydroxy(diphenyl)methyl]-5-thioxo-1,5-dihydro-4H-1,2,4-triazol-4-yl}-thiourea 4c
IR (KBr) v cm⁻¹: 3430 (OH), 3315 (NH), 3140 (Ar, CH), 1625, 1580, 1520 (C=N, C=C), 1240 (C=S). ¹H NMR (DMSO-d₆) δ ppm: 6.76 (OH, 1H, s), 7.22-7.38 (Ph, 14H, m), 10.42 (NH, 2H, s), 13.70 (triazole NH, 1H, s).

N-(3-Chlorophenyl)-N'-{3-[hydroxy(diphenyl)methyl]-5-thioxo-1,5-dihydro-4H-1,2,4-triazol-4-yl}-thiourea 4d
IR (KBr) v cm⁻¹: 3430 (OH), 3290 (NH), 3120 (Ar, CH), 1615, 1580, 1520 (C=N, C=C), 1240 (C=S). ¹H NMR (DMSO-d₆) δ ppm: 6.80 (OH, 1H, s), 7.20-7.38 (Ph, 14H, m), 10.02 (NH, 2H, s), 13.30 (triazole NH, 1H, s).

N-(4-Methylphenyl)-N'-{3-[hydroxy(diphenyl)methyl]-5-thioxo-1,5-dihydro-4H-1,2,4-triazol-4-yl}-thiourea 4e
IR (KBr) ν cm⁻¹: 3450 (OH), 3300 (NH), 3145 (Ar.CH), 1620, 1590, 1540 (C=N, C=C), 1240 (C=S). $^1$H NMR (DMSO – d₆) δ ppm: 2.6 (CH₃, 3H,s), 6.90 (OH, 1H,s), 7.25-7.36 (Ph, 1H,m), 10.03 (NH, 2H,s), 13.08 (triazole NH, 1H,s).

Synthesis of (6-Anilino-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazol-3-yl)(diphenyl)methanol 5

Equimolar amounts of 2 and an phenylisothiocyanate in dry dimethylformamide (20 ml) were refluxed for 24 h. The colorless crystalline product obtained after cooling was filtered and washed with ethanol to afford 5.

IR (KBr) ν cm⁻¹: 3450 (OH), 3300 (NH), 3100, 1615, 1585, 1570 (C=N, C=C).

$^1$H NMR(DMSO – d₆) δ ppm: 6.63 (OH, 1H,s), 7.41-7.54 (Ph, 1H,m), 9.94 (NH, 1H,s).

Results and Discussion

Absence of the C=O band of 1 at 1660 cm⁻¹ and presence of an absorption at 1615 cm⁻¹ attributed to the C=N function of the triazolinemethione system in the IR spectrum and observation of a singlet at δ 5.14 ppm (NH₂, 2H) in the NMR spectrum of 2 provided evidence for the expected transformation. The IR Spectra of 3 a-e showed characteristic bands at 3400 – 3460 cm⁻¹(OH), 3320-3200 cm⁻¹(NH), 1610-1470 cm⁻¹ (C=N; endocyclic / exocyclic and C=C), and 1035–1050cm⁻¹ (C=S) (Misra at al., 1988 and Eweiss et al., 1986). In the literature it has been stated that the sulphur at 3-position of the 1,2,4-triazole ring is said to be incorporated as a thiole (Habib et al., 1988) or thione (Eweiss et al., 1986; Ilhan et al., 1996) function. The observation of a low field NH signal (δ = 13.95 – 14.19 ppm) and a low field N=CH signal (δ = 9.32 –10.84 ppm) showed that 3 a-e existed only in the thione form.

The paramagnetic shift observed for the N=CH proton, which generally absorbs at about δ 8.50 ppm (Hesse et al., 1979), was attributed to the anisotropy of the thiocarbonyl group (Ilhan et al., 1996).

Absence of SH signals and presence of low field singlets at about δ 13.08-13.70 ppm assigned to the NH of the triazoline thione ring supported the thione form also in 4 a-e.

The IR spectrum of 5 showed OH- and NH-bands at 3451 and 3300 cm⁻¹, respectively. The structure was further confirmed by the OH singlet at δ 6.63 ppm, the multiplet at δ 7.41-7.54 ppm assigned to the aromatic protons and the characteristic broad NH peak at δ 9.94 ppm observed in the NMR spectrum.

The mass fragmentation routes of all the compounds were in accordance with the literature. (El Dawy et al., 1983; Ergenç et al., 1996).

Compound 1 did not display a molecular ion under EI whereas the quasimolecular ion (MH⁺, m/z 299, 1.3 %) was observed in the CIMS (scheme 2).
Scheme 2

3 a-e did not provide stable M⁺ peaks under electron impact and showed only low intensity quasi molecular ions (MH⁺) in the chemical ionization mass spectra. The major fragmentation route observed was the breaking of the N-N bond at 4-position of the 1,2,4-triazole ring (Ergenç et al., 1996). The proposed mass fragmentation patterns of 3 and 4a selected as examples, are presented in schemes 3 and 4 respectively.

The in vitro antimicrobial activity of 3 a - e and 4 a - e was investigated against Escherichia coli ATCC 8739, Klebsiella pneumoniae ATCC 4352, Pseudomonas aeruginosa ATCC 1539, Candida albicans ATCC 10231, Staphylococcus aureus ATCC 6538 und Staphylococcus epidermis ATCC 12228 using the Müller-Hinton medium. The following compounds inhibited the growth of S.aureus ATCC 6538 and/or S.epidermis ATCC 12228 at the cited concentrations (mcg / ml). 3c: 31.2; 3d: 31.2; 4a: 78.0; 4b: 31.2 (S.aureus ATCC 6538) and 3c:7.8; 3d: 15.6 (S.epidermis ATCC 12228).
Scheme 3
Scheme 4
Özet

4-Amino-5-[hidroksi(difenil)metil]-2,4-dihidro-3H-1,2,4-triazol-5-tiyon yapısından hareketle 5-[hidroksi (difenil)metil]-4-[(substitüte fenil)metiliden]amino]-2,4-dihidro-3H-1,2,4-triazol -3-tiyon , N-(substitüte fenil)-N'-(3-[hidroksi(difenil)metil]-5-tiyokso-1,5-dihidro-4H-1,2,4-triazol-4-il)-tiyotüre ve [1,2,4]triazolo[3,4-b] [1,3,4]tiyadiazol yapısında maddeler sentezlenerek yapılan elementel analiz ( C, H, N ) ve spektral verilerin ( IR, 1H-NMR, MS ) yardımıyla ayrıanalatılmış ve Escherichia coli ATCC 8739, Klebsiella pneumoniae ATCC 4352, Pseudomonas aeruginosa ATCC 1539, Candida albicans ATCC 10231, Staphylococcus aureus ATCC 6538 ve Staphylococcus epidermis ATCC 12228 suşlarına karşı antimikrobiyal etkileri incelenmiş ve bazı bileşiklerde S. aureus ve S. epidermis' e karşı aktive saptanmıştır ( MIK: 31.2 – 78 mcg / ml ).

References


Güler, C., Rollas, S., Kiraz, M., Ekinç, A.C. and Vidin, A. (1997). Evaluation of antimonybacterial and anticonvulsant activities of new 1-(4-fluorobenzoyl)-4-substituted-thiosemicarbazide and 5-(4-fluorophenyl)-4-substituted-2,4-dihydro-3H-1,2,4-triazole-3-thione derivatives Farmaco 52: 691-695.

Habib, N.S., Soliman, R., Ashour, F.A. and El-Taiebi, M. (1997). Synthesis and antimicrobial testing of 4H-1,2,4-triazole, 1,2,4-triazolo [3,4-b][1,3,4]thiadiazole and 1,2,4-triazolo[3,4-b] [1,3,4]thiazidazine derivatives of 1H-benzimidazole. Pharmaceutical 52: 844-847.


Received: 04.02.2002
Accepted: 10.03.2002