DESIGN, SYNTHESIS AND IN-VITRO ANTIOXIDANTEVALUATION
OF SOME NOVEL -3-[(1H-INDOL-4-YL)OXY]METHYL]-6-PHENYL-
[1,2,4]TRIAZOLO[3,4-b][1,3,4] THIADIAZOLE DERIVATIVES

Kumara Prasad S. A.*, Srinivasa U., Subrahmanyam E.V.S., Shabaraya A.R.
Srinivas College of Pharmacy, Valachil, Prangipete post, Mangalore - 574143, Karnataka, India.

ABSTRACT
A new series of 3-[(1H-indol-4-yl)oxy]methyl]-6-phenyl-
[1,2,4]triazolo[3,4-b][1,3,4] thia diazole (5) derivatives are synthesised
by the reaction of 2-[(1H-indol-4-yl)oxy] acetohydrazide (2) with
Potassium hydroxide and carbon disulfide to form 2-[(1H-indol-4-
yloxy) acetyl] hydrazinecarbodithioate (3) which on cyclization with
hydrazine hydrate and water gave 5-[(1H-indol-4-yl)oxy]methyl] -
4H-1,2,4-triazole-3-thiol (4) and these triazoles made to react with
aromatic acid in dry phosphorous oxy chloride to form the final
compounds. Finally, the structures of all the various synthesized
compounds were assigned on the basis of IR and 1H NMR spectral data
and these compounds were screened for their antioxidant activity.

KEYWORDS: Triazolo thia diazole, Aromatic acids, Antioxidant
activity.

INTRODUCTION
Recent time the research is concentrated towards the introduction of new and safe therapeutic
agents of clinical importance. The heterocycles are enjoying their importance as being the
center of activity. The nitrogen containing heterocycles are found in abundance in most of the
medicinal compounds. The success of imidazole as an important moiety of number of
medicinal agents led to introduction of the triazoles. The triazoles are said to be the isosters
of imidazoles in which the carbon atom of imidazole is isosterically replaced by nitrogen.
The history of 1, 2, 4-triazoles is more than a century old and starts with the work of Bladin\cite{1} who synthesized the first member and coined the name for this class. 1, 2, 4-triazoles are well known compounds and are found to possess varied pharmacological activities. Many of these are conveniently prepared starting from hydrazides. Analgesic, antihistaminic, diuretic, antihypertensive, anticholinergic, antibacterial, antifungal\cite{2}, anti-inflammatory\cite{3}, hypoglycemic, antitubercular, antiviral, antimicrobial\cite{4}, herbicidal, antimycotic\cite{5}, anticonvulsant\cite{6} and sedative\cite{7} properties exhibited by various 3-substituted-4-amino-5-mercapto-1, 2, 4-triazoles have made them as important chemotherapeutic agents.

Recently triazoles have been found to be intermediates for the synthesis of large number of condensed nitrogen heterocycles.\cite{9} Such findings stimulated extensive research on various substituted 1, 2, 4-triazoles.

1, 3, 4 Thiadiazole is the isomer of thiaadiazole series. Among the variety of compounds studied 1,3,4-thiadiazoles have been of great interest as antimicrobial, antitumor, diuretic, analgesic, anti-inflammatory, antioxidant and carbonic anhydrase inhibitor for several scores of years.\cite{10} At first the attention was focused on 2-aminothiadiazole and its simple derivatives. For example thiaadiazoles containing sulfonamides like Acetzolamide, Sulfaethidole, Sulfamethizole and antibacterial agents like Cefazedone, Ceftezole and Cefazolin. The literature review showed that the thiadiazole nuclei have various biological activities like anticancer\cite{11}, antimicrobial\cite{12}, anti-inflammatory\cite{13}, antifungal\cite{14} and antidepressant\cite{15} activities.

When the triazoles are condensed with thiaadiazoles yield wide range of biological and pharmacological activities, like anti-microbial agent\cite{16}, anti-inflammatory\cite{17}, antibacterial, antifungal, analgesic and diuretic agents.\cite{18} Further, these observations stimulated the extensive research on triazolo-thiadiazole nucleus with indole nucleus.

Antioxidants may be classified according to their mode of action as being free radical terminators. Chelators of metal ions involved in catalyzing lipid oxidation or oxygen scavengers that react with oxygen in closed systems.\cite{19} A number of methods are available for the determination of free radical scavenging activity but the assay employing the stable 2,2-diphenyl-1-picryl-hydrazyl radical (DPPH) has received the maximum mention owing to its ease of use amid its convenience.\cite{20} This assay is the most widely used in \textit{vitro} test to
assess free radical scavenging capacities.\cite{21} In time DPPH assay, the antioxidant activity of a compound is evaluated spectrophotometrically by monitoring the decrease in absorbance at 517 nm as DPPH (purple) transformed to the reduced form DPPH-H (yellow).

**MATERIALS AND METHODS**

All the reactions were carried out under prescribed laboratory conditions. The solvents and reagents used in the synthetic work were of laboratory reagent grade and were purified by distillation and crystallization techniques wherever necessary. The final products were purified by recrystallization. Melting points were determined by open capillary method and were uncorrected. The aromatic aldehydes were obtained commercially.

1. **Synthesis of potassium 2-[(1H-indol-4-yl)oxy] acetyl] hydrazinecarbodithioate: (3)**

   Equimolar amount of the hydrazide compound (2, 0.01 mol) and Potassium hydroxide was dissolved in absolute ethanol. Cooled the solution in ice, to this carbon disulfide was added in small portions with constant stirring. The reaction mixture was agitated continuously for a period of 15 hrs. It was then diluted with anhydrous ether. The precipitated potassium dithiocarbazinate was collected by filtration. The precipitate was further washed with anhydrous ether and dried under vacuum. The potassium salt thus obtained was in quantitative yield and was used in the next step without further purification.

2. **Synthesis of 5-(((1H-indol-4-yl)oxy)methyl)-4-amino-1,2,4-triazole-3-thiol (4)**

   A suspension of potassium dithiocarbazinate of respective aromatic esters in water and hydrazine hydrate was refluxed for 6-7hrs. With occasional shaking, the colour of the reaction mixture changed to green with the evolution of hydrogen sulfide gas. A homogenous reaction mixture was obtained during the reaction process. The reaction mixture was cooled to room temperature and diluted with water. On acidification with concentrated hydrochloric acid, the required triazole was precipitated. It was filtered, washed thoroughly with cold water and recrystallized from ethanol. The completion of reaction was monitored on TLC by using silica gel-G coated plates by using ethyl acetate and petroleum ether as the eluent and observed in UV light.

3. **Synthesis of 3-(((1H-indol-4-yl)oxy)methyl)-6-phenyl- [1,2,4]triazolo [3,4-b] [1,3,4] thiadiazole (5a-j)**

   An equimolar mixture of the respective triazole, aromatic acid in dry phosphorous oxy chloride was refluxed for 7hrs. The reaction mixture was cooled to room temperature and
then gradually poured onto crushed ice with stirring. Finely powdered potassium carbonate and the required amount of solid potassium hydroxide were added till the pH of the mixture was raised to 8, to remove the excess of phosphorous oxychloride. The mixture was allowed to stand overnight and the solid was separated. It was filtered washed thoroughly with cold water, dried and recrystallized from hot ethanol.

Table 1: List of triazolo-thiadiazole derivatives (5a-j)

<table>
<thead>
<tr>
<th>Compound</th>
<th>IUPAC Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>5a</td>
<td>3-(((1H-indol-4-yl)oxy)methyl)-6-phenyl-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazole</td>
</tr>
<tr>
<td>5b</td>
<td>3-((3-(((1H-indol-4-yl)oxy)methyl)-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazol-6-yl)phenol</td>
</tr>
<tr>
<td>5c</td>
<td>3-(((1H-indol-4-yl)oxy)methyl)-6-(4-chlorophenyl)_[1,2,4]triazolo[3,4-b][1,3,4]thiadiazole</td>
</tr>
<tr>
<td>5d</td>
<td>3-(((1H-indol-4-yl)oxy)methyl)-6-(4-methoxyphenyl)-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazole</td>
</tr>
<tr>
<td>5e</td>
<td>3-(((1H-indol-4-yl)oxy)methyl)-6-(2-bromophenyl)_[1,2,4]triazolo[3,4-b][1,3,4]thiadiazole</td>
</tr>
<tr>
<td>5f</td>
<td>3-(((1H-indol-4-yl)oxy)methyl)-6-(2-chloro-4-nitrophenyl)-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazole</td>
</tr>
<tr>
<td>5g</td>
<td>3-(((1H-indol-4-yl)oxy)methyl)-6-(2,4-dichlorophenyl)-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazole</td>
</tr>
<tr>
<td>5h</td>
<td>3-(((1H-indol-4-yl)oxy)methyl)-6-(3,5-dinitrophenyl)_[1,2,4]triazolo[3,4-b][1,3,4]thiadiazole</td>
</tr>
<tr>
<td>5i</td>
<td>3-(((1H-indol-4-yl)oxy)methyl)-6-(3,5-dimethoxyphenyl)-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazole</td>
</tr>
<tr>
<td>5j</td>
<td>4-(((1H-indol-4-yl)oxy)methyl)-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazol-6-yl]benzene-1,3-diol</td>
</tr>
</tbody>
</table>

Table 2: Physical constants data of synthesized compounds:

<table>
<thead>
<tr>
<th>Compound</th>
<th>R</th>
<th>Mol. formula</th>
<th>% yield</th>
<th>Rf</th>
<th>m.p.</th>
</tr>
</thead>
<tbody>
<tr>
<td>5a</td>
<td>H</td>
<td>C_{18}H_{15}N_{5}OS</td>
<td>68</td>
<td>0.68</td>
<td>141</td>
</tr>
<tr>
<td>5b</td>
<td>4-OH</td>
<td>C_{18}H_{13}N_{5}O_{2}S</td>
<td>72</td>
<td>0.76</td>
<td>162</td>
</tr>
<tr>
<td>5c</td>
<td>4-Cl</td>
<td>C_{18}H_{12}ClN_{2}O_{2}S</td>
<td>66</td>
<td>0.54</td>
<td>171</td>
</tr>
<tr>
<td>5d</td>
<td>4-OCH_{3}</td>
<td>C_{19}H_{14}N_{5}O_{2}S</td>
<td>78</td>
<td>0.72</td>
<td>183</td>
</tr>
<tr>
<td>5e</td>
<td>2-Br</td>
<td>C_{18}H_{11}BrN_{5}OS</td>
<td>80</td>
<td>0.70</td>
<td>222</td>
</tr>
<tr>
<td>5f</td>
<td>2,4- (Cl)_{2}</td>
<td>C_{18}H_{11}BrN_{5}OS</td>
<td>62</td>
<td>0.61</td>
<td>177</td>
</tr>
<tr>
<td>5g</td>
<td>3,5- (NO_{2})_{2}</td>
<td>C_{18}H_{11}N_{7}O_{5}S</td>
<td>83</td>
<td>0.52</td>
<td>189</td>
</tr>
<tr>
<td>5h</td>
<td>3,5- (OCH_{3})_{2}</td>
<td>C_{20}H_{17}N_{5}O_{3}S</td>
<td>75</td>
<td>0.84</td>
<td>213</td>
</tr>
<tr>
<td>5i</td>
<td>2-Cl, 4-NO_{2}</td>
<td>C_{18}H_{11}Cl N_{6}O_{3}S</td>
<td>64</td>
<td>0.48</td>
<td>203</td>
</tr>
<tr>
<td>5j</td>
<td>2,4-(OH)_{2}</td>
<td>C_{18}H_{13}N_{4}O_{3}S</td>
<td>88</td>
<td>0.66</td>
<td>156</td>
</tr>
</tbody>
</table>

SPECTRAL DATA OF SYNTHESIZED COMPOUNDS

3-(((1H-indol-4-yl)oxy)methyl)-6-phenyl-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazole (5a)

IR (KBr) cm\(^{-1}\): 3115, 3006, 2973, 2804, 1581,1467, 1389, 1238, 1154, 1063, 914, 822, 770.

\(^1\)H NMR (DMSO D\(_6\), 400 MHz) ppm 8.74-6.14 (m, 11H, Ar), 4.84 (s, 2H, OCH\(_2\)) ,136-150
(triazolo-thiadiazole).

3-(3-((1H-indol-4-yl)oxy)methyl-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazol-6-yl)phenol (5b): IR (KBr) cm⁻¹ 3094, 3005, 2968, 2815, 1559, 1476, 1381, 1266, 1163, 1078, 935, 821, 786. ¹H NMR (DMSO D₆, 400 MHz) ppm 8.32-6.38 (m, 10H, Ar), 5.16 (s, 2H, OCH₂), 135-149 (triazolo-thiadiazole).

3-(((1H-indol-4-yl)oxy)methyl)-6-(4-chlorophenyl)-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazole (5c): IR (KBr) cm⁻¹ 3118, 3026, 2951, 2833, 1567, 1504, 1486, 1389, 1256, 1166, 1075, 938, 822, 774 ¹H NMR (DMSO D₆, 400 MHz) ppm 8.43-6.27 (m, 10H, Ar), 5.16 (s, 2H, OCH₂), 134-152 (triazolo-thiadiazole).

3-(((1H-indol-4-yl)oxy)methyl)-6-(4-methoxyphenyl)-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazole (5d): IR (KBr) cm⁻¹ 3117, 3020, 2953, 2858, 1371, 1341, 1558, 1525, 1481, 1387, 1354, 1254, 1151, 1066, 934, 813, 771. ¹H NMR (DMSO D₆, 400 MHz) ppm 8.64-6.52 (m, 11H, Ar), 5.08 (s, 2H,OCH₂), 3.52 (b, s, 1H, OH), 134-148 (triazolo-thiadiazole).

3-(((1H-indol-4-yl)oxy)methyl)-6-(2-bromophenyl)-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazole (5e): IR (KBr) cm⁻¹ 3431, 3134, 3026, 2967, 2848, 1359, 1368, 1555, 1567, 1483, 1356, 1324, 1265, 1149, 1062, 925, 817, 773 ¹H NMR (DMSO D₆, 400 MHz) ppm 8.56-6.42 (m, 10H, Ar), 5.08 (s, 2H, OCH₂), 3.52 (b, s, 1H, OH), 134-148 (triazolo-thiadiazole).

3-(((1H-indol-4-yl)oxy)methyl)-6-(2-chloro-4-nitrophenyl)-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazole (5f): IR (KBr) cm⁻¹ 3113, 3017, 2969, 2852, 1376, 1345, 1562, 1511, 1475, 1387, 1358, 1262, 1159, 1066, 925, 813, 763. ¹H NMR (DMSO D₆, 400 MHz) ppm 8.51-6.42 (m, 10H, Ar), 5.03 (s, 2H, OCH₂), 2.53 (s, 3H, CH₃), 135-149 (triazolo-thiadiazole).

3-(((1H-indol-4-yl)oxy)methyl)-6-(2,4-dichlorophenyl)-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazole (5g): IR (KBr) cm⁻¹ 3119, 3025, 2958, 2862, 1386, 1368, 1542, 1515, 1468, 1373, 1351, 1253, 1157, 1058, 926, 813, 771. ¹H NMR (DMSO D₆, 400 MHz) ppm 8.42-6.34 (m, 10H, Ar), 5.04 (s, 2H, OCH₂), 4.04 (b, s, 1H, OH), 133-146 (triazolo-thiadiazole).

3-(((1H-indol-4-yl)oxy)methyl)-6-(3,5-dinitrophenyl)-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazole (5h): IR (KBr) cm⁻¹ 3114, 3017, 2968, 2878, 1384, 1367, 1562, 1529, 1459, 1378, 1364, 1259, 1153, 1067, 937, 818, 778. ¹H NMR (DMSO D₆, 400 MHz) ppm
8.48 -6.54 (m, 10 H, Ar), 5.07 (s, 2H, OCH\(_2\)), 2.23 (s, 6H, -N(CH\(_3\))\(_2\)), 135-148 (triazolo-thiadiazole).

3-(((1H-indol-4-yl)oxy)methyl)-6-(3,5-dimethoxyphenyl)\([1,2,4]\)triazolo\([3,4-b]\)\([1,3,4]\)thiadiazole (5i): IR (KBr) cm\(^{-1}\) 3350, 3128, 3012, 2979, 2884, 1377, 1353, 1558, 1513, 1452, 1387, 1362, 1257, 1149, 1050, 921, 812, 787. \(^1\)H NMR (DMSO D\(_6\), 400 MHz) ppm 8.65 -6.53 (m, 9H, Ar), 4.97 (s, 2H, OCH\(_2\)), 4.43 (b, s, 1H, -3-OH of phenyl), 3.91 (s, 3H, 4-OCH\(_3\) of phenyl), 137-154 (triazolo-thiadiazole).

4-(((3-(((1H-indol-4-yl)oxy)methyl)\([1,2,4]\)triazolo\([3,4-b]\)\([1,3,4]\)thiadiazol-6-yl)benzene-1,3-diol (5j): IR (KBr) cm\(^{-1}\) 3126, 3027, 2944, 2872, 1386, 1358, 1543, 1526, 1452, 1382, 1355, 1268, 1152, 1054, 932, 817, 782. \(^1\)H NMR (DMSO D\(_6\), 400 MHz) ppm 8.62-5.64 (m, 9 H, Ar), 4.83 (s, 2H, OCH\(_2\)), 3.41 (s, 6H, -OCH\(_3\))\(_2\)), 134-147 (triazolo-thiadiazole).

IN VITRO ANTIOXIDANT EVALUATION BY DIPHENYL-2-PICRYLHYDRAZYL (DPPH) SCAVENGING EFFECT

**Chemicals and Instruments:** All chemicals and solvents used in the study were of analytical grade. DPPH (HIMEDIA), India. Phenazine methosulfate (PMS) and thiobarbituric acid (TBA) were obtained from Loba Chemie Mumbai, India. Nitroblue tetrazolium (NBT) (HIMEDIA), India, Butylated Hydroxy Toluene (BHT), Nicotinamide Adenine Dinucleotide (NADH) was obtained from Lobo Chemie, Mumbai. Trichloroacetic acid (TCA) and potassium chloride were obtained from Karnataka Fine Chemicals, India. UV spectrophotometer (Shimadzu 2450), homogenizer, centrifuge (Remi, India) and pH meter (Elico Ltd., India) were the instruments used for the study.

**Preparation of Stock Solutions:** The stock solutions were prepared by dissolving 100 mg of synthesised compounds in 100 ml of methanol to make a stock solution of 1 mg/ml. Aliquots from this stock solution were further diluted with methanol to get the final concentrations viz. 10, 20, 40, 60, 80 and 100 µg/ml.

**Preparation of Ascorbic Acid Stock Solution:** Ascorbic acid stock solution was prepared in the concentration of 1mg/ml in water. From the stock solution different concentrations viz. 10, 20, 40, 60, 80 and 100 mg/ml were prepared in water and used for antioxidant studies.

Reactions were performed in 1.25ml of methanol containing 0.5nm freshly made DPPH and various concentrations of the synthesized compound and ascorbic acid. Reaction mixture was
incubated at 37°C for 30 min. and the absorbance was measured at 517 nm. The percentage increase in absorbance was measured by comparing the absorbance values of control and those of test compound. The percentage inhibition of antiradical activity was calculated using the formula,

\[
\text{% inhibition} = \left( \frac{\text{Absorbance of blank} - \text{Absorbance of test sample}}{\text{Absorbance of blank}} \right) \times 100
\]

RESULTS AND DISCUSSION

The radical scavenging activity (RSA) for ethanolic solutions of title compounds 5 a-j are presented in Table 3 and compared with that of standard Ascorbic acid. The results in percentage are expressed as the ratio of absorbance decrease at 517 nm and the absorbance of DPPH solution in the absence of test and standards. The analysis of Table 3 leads us to conclude that the RSA of title compounds on DPPH radicals increases with the increase in concentration. Compounds 5 a-j showed excellent radical scavenging activity (81-93%) at 100µg/ml concentration. Compound 5b showed highest activity (93.67%) at 100µg/ml. The radical scavenging activity of compound 4a, 5i and 5j were slightly less potent than the standards and other compounds. All other compounds 5b-5h exhibited more potent radical scavenging activities at concentration 100µg/ml. At concentrations greater than 100µg/ml the radical scavenging activity for all the compounds exceeded the maximum limit.

Table 3: DPPH free radical scavenging activity

<table>
<thead>
<tr>
<th>Compounds</th>
<th>Concentration µg/ml</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>10</td>
</tr>
<tr>
<td>Standard</td>
<td>25.76</td>
</tr>
<tr>
<td>5a</td>
<td>16.17</td>
</tr>
<tr>
<td>5b</td>
<td>25.06</td>
</tr>
<tr>
<td>5c</td>
<td>22.93</td>
</tr>
<tr>
<td>5d</td>
<td>23.50</td>
</tr>
<tr>
<td>5e</td>
<td>20.74</td>
</tr>
<tr>
<td>5f</td>
<td>19.17</td>
</tr>
<tr>
<td>5g</td>
<td>21.47</td>
</tr>
<tr>
<td>5h</td>
<td>23.36</td>
</tr>
<tr>
<td>5i</td>
<td>17.42</td>
</tr>
<tr>
<td>5j</td>
<td>18.08</td>
</tr>
</tbody>
</table>
CONCLUSION

In the present study, series of triazolo-thiazole derivatives from 4-hydroxy indole have been synthesized and confirmed through the spectral data. Further, they have been screened for in-vitro antioxidant activity by Diphenyl-2-Picrylhydrazyl (DPPH) Scavenging effect. It was concluded that these synthesized compounds have the potential of being useful in the treatment of such disorders for which they have been screened in the present study.

ACKNOWLEDGEMENT

The authors wish to thank Management of Srinivas College of Pharmacy, Valachil, Mangalore for the necessary facilities and encouragement. Also thanks to Indian Institute of Sciences, Bangalore for carrying out IR, HNMR and mass spectra.

REFERENCES

3. Paresh JK, Mark AM, Shiva PS, Surendra SP, Virgil IS. Synthesis of 5-(1-


5. Bing Chai, Xuhong Qian, Song Cao, Haidong Liu, Gonghua Song. Synthesis and insecticidal activity of 1, 2, 4-triazole derivatives. Arkivoc 2003; 2: 141-145.


7. Li-Ping Guan, Qing-Hao Jin, Guan-Rong Tian, Kyu-Yun Chai, and Zhe-Shan Quan, Synthesis of some quinoline-2(1H)-one and 1, 2, 4 - triazole [4,3-a]quinoline derivatives as potent anticonvulsants. J Pharm Sci. 2007; 10(3): 254-262.


9. Gadag RV, Gajendragad MR. 4-Amino-3-methyl-5-mercapto-1, 2, 4-triazole as a gravimetric reagent for determination of silver in silver compounds. Talanta 1978; 25(7): 418-420.


16. Mogilaiah K, Ramarao G and Sreenivасulu, Synthesis and antimicrobial activity of 1, 2,4-triazolyl / 1,3,4- thiadiazolyl/ 1,3,4- oxadiazolyl- 1, 8- naphthyridines and related compounds. Ind. J Chem. 1996; 35B: 339-344.

17. Mohd Amir and Rajesh Agarwal, Synthesis and anti-inflammatory activity of 5-(8-Quinolinoxy methyl)-1,3,4- oxadiazole/ 1,3,4- Thia diazole and 1,2,4- (H) Triazole. Ind J Heter Chem. 1998; 7: 225-228.

18. Srivastava SK, Soumya Srivastava and Srivastava SD. Synthesis of 5-arylidene-2-aryl-3-(1,2,4- triazoloacetamidyl)-1, 3-thiadiazol-4-ones as antibacterial, antifungal, analgesic and diuretic agents. Ind J Chem. 2002; 41B: 1937-1945.


26. Karabasanagouda T, Vasudeva AA, Suchetha NS. Synthesis and antimicrobial activities of some novel 1,2,4-triazolo [3,4-b]-1,3,4-thiadiazoles and 1,2,4-tria zolo[3,4-b]-1,3,4-thiadiazines carrying thioalkyl and sulphonyl phenoxy moieties. Euro J of Med Chem. 2007; 42: 521-529.


29. Pintilie O, Lenuta P, Valeriu S, Marcel P, Aurel Pui. Synthesis and antimicrobial activity of some new 1,3,4- Thiadiazole and 1,2,4-Triazole Compounds having a D,L-Methionine