

CONTENTS

Certificate i
Approval Sheet ii
Declaration iii
Acknowledgement iv
Abstract v
List of Figure xiii
List of Table xvi
List of Symbols and Abbreviation xviii

<table>
<thead>
<tr>
<th>Chapters</th>
<th>Particulars</th>
<th>Page No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>INTRODUCTION</td>
<td>1-7</td>
</tr>
<tr>
<td>2</td>
<td>LITERATURE REVIEW</td>
<td>8-24</td>
</tr>
<tr>
<td>2.1</td>
<td>History and development of sulfonylurea</td>
<td>8</td>
</tr>
<tr>
<td>2.2</td>
<td>Biological activity sulfonylurea and related compounds</td>
<td>9</td>
</tr>
<tr>
<td>3</td>
<td>MATERIAL AND METHODOLOGY</td>
<td>26-58</td>
</tr>
<tr>
<td>3.1</td>
<td>Instruments and chemicals</td>
<td>26</td>
</tr>
<tr>
<td>3.2</td>
<td>UV-visible spectrophotometry</td>
<td>26</td>
</tr>
<tr>
<td>3.3</td>
<td>Infrared spectroscopy</td>
<td>27</td>
</tr>
<tr>
<td>3.4</td>
<td>(^1)H NMR spectroscopy</td>
<td>27</td>
</tr>
<tr>
<td>3.5</td>
<td>Gas chromatography/mass spectrometry (GC-MS)</td>
<td>27</td>
</tr>
<tr>
<td>3.6</td>
<td>Experimental methods of synthesis</td>
<td>28</td>
</tr>
<tr>
<td>3.6.1</td>
<td>Synthesis of 1-(4-(4,6-dimethyl-6H-1,3-thiazin-2-yl)phenylsulfonyl)-3-substituted-1-(substituted)urea/thiourea (5a-o and 6a-e) (scheme-I)</td>
<td>28</td>
</tr>
<tr>
<td>3.6.1.1</td>
<td>Procedure for synthesis of 4,6-dimethyl-2-phenyl-2H-1,3-thiazine (1)</td>
<td>30</td>
</tr>
<tr>
<td>3.6.1.2</td>
<td>Procedure for synthesis of 4-(4,6-dimethyl-6H-1,3-thiazin-2-yl)benzene-1-sulfonyl chloride (2)</td>
<td>31</td>
</tr>
<tr>
<td>3.6.1.3</td>
<td>Procedure for synthesis of 4-(4,6-dimethyl-6H-1,3-thiazin-2-yl)-N-substituted benzenesulfonyamide (3a-c)</td>
<td>31</td>
</tr>
</tbody>
</table>
3.6.1.4 Procedure for the synthesis of Ethyl 4-(4,6-dimethyl-6H-1,3-thiazin-2-yl)phenylsulfonyl(substituted) carbamate (4a-c)

3.6.1.5 General procedure for the synthesis of 1-(4-(4,6-dimethyl-6H-1,3-thiazin-2-yl)phenylsulfonyl)-3-substituted-1-(substituted)urea (5a-o)

3.6.1.6 Procedure for synthesis of 1-(4-substitutedphenyl)-3-(4-(4,6-dimethyl-6H-1,3-thiazin-2-yl)phenylsulfonyl)urea/thiourea (6a-l)

3.6.2 Synthesis of 1-(substituted phenyl)-3-(4-(4,6-dimethyl-6H-1,3-thiazin-2-yl)phenylsulfonyl)urea/thiourea (6a-l)

3.6.2.1 Procedure for synthesis of 2,4-thiazolidinedione (1)

3.6.2.2 Procedure for synthesis of 5-benzylidenethiazolidine-2,4-dione (2)

3.6.2.3 Procedure for synthesis of 4-(2,4-diozothiazolidin-5-ylidene)methyl)benzene-1-sulfonyl chloride (3)

3.6.2.4 Procedure for synthesis of 4-(2,4-diozothiazolidin-5-ylidene)methyl)-N-(pyridin-2-yl)benzenesulfonamide (4)

3.6.2.5 Procedure for synthesis of ethyl 4-(2,4-diozothiazolidin-5-ylidene)methyl)phenylsulfonyl(pyridin-2-yl)carbamate (5)

3.6.2.6 Procedure for synthesis of 3-(4-substitutedphenyl)-1-(4-(2,4-diozothia-zolidin-5-ylidene)methyl)phenylsulfonyl)-1-(pyridin-2-yl)urea (6i-v)

3.6.2.7 Procedure for synthesis of 1-(substituted-phenyl)-3-(4-(2,4-diozothia zolidin-5-ylidene) methyl)phenyl-sulfonyl)urea/thiourea (7i-x)

3.6.3 Synthesis of 1-(substituted)-3-(4-(3,5-dimethyl-1H-pyrazol-1-yl)phenylsulf -onyl)urea (3i-viii) (scheme-III)

3.6.3.1 Procedure for synthesis of 3,5-dimethyl-1-phenyl-1H-pyrazole (1)

3.6.3.2 Procedure for synthesis of 4-(3,5-dimethyl-1H-pyrazol-1-yl)benzene-1-sulfonly chloride (2)

3.6.3.3 General procedure for synthesis of 1-(3/4-substitutedphenyl)-3-(4-(3,5-dimethyl-1H-pyrazol-1-yl)phenylsulfonyl)urea (3i-viii)

3.7 Experimental procedure for biological activity

3.7.1 Animals
3.7.2 Acute toxicity study 56
3.7.3 Study of alloxan induced non-insulin dependent diabetes mellitus (NIDDM) in rats 56
3.7.4 Oral glucose tolerance test (OGTT) 57
3.7.5 Anticonvulsant activity 57
3.7.5.1 Maximal electroshock Seizure (MES) model 57
3.7.5.2 Pentylenetetrazole (PTZ) induced seizure test 58
3.7.5.3 Neurotoxicity screening 58
3.8 In silico study 58

4 RESULT AND DISCUSSION 59-120
4.1 Synthesis of 1-(4-(4,6-dimethyl-6H-1,3-thiazin-2-yl)phenylsulfonyl)-3-substituted-1-(substituted)urea (5a-o) analogues 59
4.1.1 FT/IR spectral characterization 61
4.1.2 1H NMR spectral characterization 63
4.1.3 GC-MS studies 66
4.1.4 UV-visible spectroscopy 67
4.1.5 Acute oral toxicity 67
4.1.6 Antidiabetic study 68
4.1.7 Oral glucose tolerance test (OGTT) 70
4.1.8 Neurotoxicity study 72
4.1.9 Anticonvulsant study 72
4.1.10 In silicon study 73
4.2 Synthesis of 1-(4-substitutedphenyl)-3-(4-(4,6-dimethyl-6H-1,3-thiazin-2-yl)phenylsulfon)urea/thiourea (6a-l) analogues 75
4.2.1 FT/IR spectral characterization 76
4.2.2 1H NMR spectral characterization 77
4.2.3 GC-MS studies 79
4.2.4 UV-visible spectroscopy 80
4.2.5 Acute oral toxicity 81
4.2.6 Antidiabetic study 81
4.2.7 Oral glucose tolerance test (OGTT) 83
4.2.8 Neurotoxicity study 83
4.2.9 Anticonvulsant study 84
4.2.10 In silicon study 85
4.3 Discussion 86
4.4 Synthesis of 3-(4-substitutedphenyl)-1-(4-((2,4-dioxothiazolidin-5-ylidene)-methyl)phenylsulfonyl)-1-(pyridin-2-yl)urea (6i-v) analogues 88
4.4.1 FT/IR spectral characterization 89
4.4.2 $^1$H NMR spectral characterization 90
4.4.3 GC-MS studies 91
4.4.4 UV-visible spectroscopy 92
4.4.5 Acute oral toxicity 93
4.4.6 Antidiabetic study 93
4.4.7 Oral glucose tolerance test (OGTT) 94
4.4.8 Neurotoxicity study 95
4.4.9 Anticonvulsant study 95
4.4.10 In silicon study 97
4.5 Synthesis of 1-(substituted-phenyl)-3-(4-((2,4-dioxothiazolidin-5-ylidene) methyl)phenyl-sulfonyl)urea/thiourea (7i-x) analogues 97
4.5.1 FT/IR spectral characterization 98
4.5.2 $^1$H NMR spectral characterization 100
4.5.3 GC-MS studies 101
4.5.4 UV-visible spectroscopy 102
4.5.5 Acute oral toxicity 103
4.5.6 Antidiabetic study 103
4.5.7 Oral glucose tolerance test (OGTT) 104
4.5.8 Neurotoxicity study 105
4.5.9 Anticonvulsant study 105
4.5.10 In silicon study 107
4.6 Discussion 108
4.7 Synthesis of 1-(aryl/heteroaryl)-3-(4-(3,5-dimethyl-1H-pyrazol-1-yl)phenylsulfonyl)urea (3i-viii) analogues 109
4.7.1 FT/IR spectral characterization 110
4.7.2 $^1$H NMR spectral characterization 111
4.7.3 GC-MS studies .......................................................... 112
4.7.4 UV-visible spectroscopy ........................................... 113
4.7.5 Acute oral toxicity ................................................. 114
4.7.6 Antidiabetic study .................................................. 114
4.7.7 Oral glucose tolerance test (OGTT) ......................... 116
4.7.8 Neurotoxicity study .............................................. 116
4.7.9 Anticonvulsant study ............................................ 117
4.7.10 In silicon study .................................................... 118
4.8 Discussion .......................................................... 120
5 CONCLUSION ......................................................... 121-124
6 FUTURE PROSPECT ..................................................... 125
      Reference ............................................................ 126-133
      List of publications ............................................. 134
      Appendix .......................................................... 135