ABSTRACT

The thesis entitled *Synthesis, characterization and biological activity of some new N/N-S containing heterocyclic compound* is fully devoted to the study of the heterocyclic compounds. The thesis describes the synthesis, characterization and biological activity of some new heterocyclic compounds derived from 1, 2, 3-benzotriazole and 1H-Indole nucleus. The thesis has been divided into five chapters. Each chapter has its own significance with regards to the characterization and explanation of the subject concern.

CHAPTER-1:

This chapter highlights several aspects related to heterocyclic compounds such as definition, classification and their biological significance, including their uses in industry, agriculture and pharmaceutics.

CHAPTER-2:

This chapter has been divided into four sections 2.1, 2.2, 2.3 and 2.4 respectively.

SECTION 2.1: This section includes a brief description of the literature survey and biological importance of 1,2,3-benzotriazole and related compounds. 1,2,3-Benzotriazole has its synthetic value for its numerous applications in industry and agriculture. It has an important place in
Abstract
dystuffs, optical brightness, fluorescents, corrosion inhibitors, agrochemicals
and photostabilizer. 1,2,3-Benzotriazole derivatives have also their important
place in therapeutics as a bactericide, antiinflammatory, antitumor,
fungicides, antidepressant, muscle relaxant and antineoplastic agent.

SECTION 2.2: This section describes a brief description of the literature
survey and biological importance of 1H-indole and related compounds.
1H-indole derivatives find a large number of uses as colouring agent,
essential amino acid, plant growth hormones and in blood sugar lowering
agents. 1H-indole derivatives has also their important place in the
therapeutics as antibiotic, antitumor, treatment of hypertention, and
tranquillizer. 1H-indole derivatives are also reported in agrochemical
fields as insecticides, nematicides and acaricides.

SECTION 2.3: This section represents a brief description of the literature
survey and biological importance of azetidinones nucleus. Staudinger,
before 1912, initiated the work on the chemistry of 2-azetidinones or β-
lactam. Interest in this compounds was largely lost until 1943 when it was
suggested that the penicillin might contain azetidinone ring. Since then a
great deal of work has been done on this compound. A large number of
antibiotics contain azetidinones moiety. The reactivity of azetidinones
influences largely on substitution. 2-Azetidinones and its derivatives
possess variety of therapeutical activities such as antimicrobial,
antiparkinsonian, antitubercular and antitirrigidity activities.
SECTION 2.4: This section describes the aim and work plan of the research work.

There are three main objectives of the research plan.

1. To synthesise the new heterocyclic compounds.
2. To characterisation their structures by microanalytical data and spectral methods and
3. To evaluate their biological activity viz.
   a: Antibacterial.
   b: Antifungal.
   c: Antiinflammatory and
   d: Anticonvulsant.

Four series 1,2,3 and 4 of the compounds have been synthesized by following the schemes 1,2 and 3 respectively.

Series-1: \(N^1\)-[\(\alpha\)-(substituted arylidenehydrazino)-acetyl]-1,2,3-benzotriazole.

Series-2: \(N^1\)-[\(\alpha\)-(4-substituted aryl-3-chloro-2-oxo-1-azetidinyl amino)acetyl]-1,2,3-benzotriazole.

Series-3: \(N^1\)-[\(\alpha\)-(substituted arylidenehydrazino)-acetyl]-1H-indole.

Series-4: \(N^1\)-[\(\alpha\)-(4-substituted aryl-3-chloro-2-oxo-1-azetidinyl amino)acetyl]-1H-indole.
Scheme-1

\[
\begin{align*}
\text{Het} & \quad \text{NH} \\
\rightarrow & \quad \text{ClCOCH}_2\text{Cl} \\
\text{Het} & \quad \text{NCOCH}_2\text{Cl} \\
1 & \quad \text{NH}_2\text{NH}_2 \\
\rightarrow & \quad \text{Het} \quad \text{NCOCH}_2\text{NHNH}_2 \\
2 & \quad \text{O} = \text{C} \quad \text{Ar} \\
\rightarrow & \quad \text{Het} \quad \text{NCOCH}_2\text{NHN} = \text{C} \quad \text{Ar} \\
3 & \quad \text{ClCOCH}_2\text{Cl} \\
\rightarrow & \quad \text{Het} \quad \text{NCOCH}_2\text{NH} \quad \text{N} \quad \text{C} \quad \text{H} \quad \text{Cl} \\
\text{where} & \\
\text{Het} \quad \text{NH} & = 1,2,3\text{-benzotriazole} / 1H\text{-indole} \\
\text{R} & = \text{H} / \text{alkyl} \\
\text{Ar} & = \text{Aryl} / \text{substituted aryl}
\end{align*}
\]
CHAPTER-3:

This chapter has been divided into two sections 3.1 and 3.2 respectively.

SECTION 3.1:

Series 1: Synthesis and characterization of $N^1$-[α-(substituted arylidenehydrazino)-acetyl]-1,2,3-benzotriazole, SG 3-12.

Synthetic Procedure: A brief description of the synthesis of the compounds is given below:

Equimolar solution of 1,2,3-benzotriazole and chloroacetyl chloride in the presence of triethyl amine in dioxane was refluxed on a water bath to give $N^1$-chloroacetyl -1, 2, 3-benzotriazole, compound SG 1. The compound SG 1 was reacted with hydrazine hydrate to produce $N^1$-(Hydrazinoacetyl)-1, 2, 3-benzotriazole, compound SG 2. The compound SG 2 on condensation with various carbonyls (TABLE-1) afforded compounds SG 3-12 (Scheme 2).

Characterization of the compounds SG 1-12: The synthesized compounds SG 1-12 were characterized by chromatographic techniques, elemental analysis and spectral data. The melting points of the compounds SG 1-12 were determined by open capillary method.

The following structures have been drawn for the synthesized compounds SG 3-12.
Scheme-2

$\text{Scheme-2}$

$\text{COCH}_2\text{Cl}$

$\text{COCH}_2\text{Cl}$

$\text{NH}_2\text{NNH}_2$

$\text{COCH}_2\text{NNNH}_2$

$\text{COCH}_2\text{NH} \equiv \text{C}$

$\text{COCH}_2\text{Cl}$

$\text{COCH}_2\text{NH} \equiv \text{C}$
TABLE- 1

<table>
<thead>
<tr>
<th>Compound</th>
<th>Ar</th>
<th>R</th>
<th>Molecular formula</th>
</tr>
</thead>
<tbody>
<tr>
<td>SG 3</td>
<td>-C₆H₅</td>
<td>-H</td>
<td>C₁₅H₁₃N₅O</td>
</tr>
<tr>
<td>SG 4</td>
<td>2-CIC₆H₄</td>
<td>-H</td>
<td>C₁₅H₁₂N₅OCl</td>
</tr>
<tr>
<td>SG 5</td>
<td>4-CIC₆H₄</td>
<td>-H</td>
<td>C₁₅H₁₂N₅OCl</td>
</tr>
<tr>
<td>SG 6</td>
<td>2-CIC₆H₄</td>
<td>-CH₃</td>
<td>C₁₆H₁₄N₅OCl</td>
</tr>
<tr>
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<td>-CH₃</td>
<td>C₁₆H₁₄N₅OCl</td>
</tr>
<tr>
<td>SG 8</td>
<td>2-BrC₆H₄</td>
<td>-H</td>
<td>C₁₅H₁₂N₅OBr</td>
</tr>
<tr>
<td>SG 9</td>
<td>2-OHC₆H₄</td>
<td>-H</td>
<td>C₁₅H₁₃N₅O₂</td>
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<tr>
<td>SG 10</td>
<td>4-OHC₆H₄</td>
<td>-H</td>
<td>C₁₅H₁₃N₅O₂</td>
</tr>
<tr>
<td>SG 11</td>
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<td>-CH₃</td>
<td>C₁₆H₁₅N₅O₂</td>
</tr>
<tr>
<td>SG 12</td>
<td>4-OHC₆H₄</td>
<td>-CH₃</td>
<td>C₁₆H₁₅N₅O₂</td>
</tr>
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</table>

SECTION 3.2:

Series 2: Synthesis and characterization of N¹-[α-(4-substituted aryl-3-chloro-2-oxo-1-azetidinyl amino)-acetyl]-1,2,3-benzotriazole, SG 13-22.

Synthetic procedure: The compounds SG 3-12 of series 1 on reaction with chloroacetyl chloride in presence of triethyl amine in dioxane yielded compounds SG 13-22 (TABLE-2) (Scheme-2).
Characterization of the compounds SG 13-22: The synthesized compounds SG 13-22 were characterized by chromatographic methods, elemental analysis and spectral data. The melting points of the compounds SG 13 - 22 were determined by open capillary method.

The following structures have been drawn for the synthesized compounds SG 13-23.

![Chemical structure](image)

**TABLE-2**

<table>
<thead>
<tr>
<th>Compounds</th>
<th>Ar</th>
<th>R</th>
<th>Molecular formula</th>
</tr>
</thead>
<tbody>
<tr>
<td>SG 13</td>
<td>-C₆H₅</td>
<td>-H</td>
<td>C₁₇H₁₄N₅O₂Cl</td>
</tr>
<tr>
<td>SG 14</td>
<td>2-CIC₆H₄</td>
<td>-H</td>
<td>C₁₇H₁₃N₅O₂Cl₂</td>
</tr>
<tr>
<td>SG 15</td>
<td>4-CIC₆H₄</td>
<td>-H</td>
<td>C₁₇H₁₃N₅O₂Cl₂</td>
</tr>
<tr>
<td>SG 16</td>
<td>2-CIC₆H₄</td>
<td>-CH₃</td>
<td>C₁₈H₁₅N₅O₃Cl₂</td>
</tr>
<tr>
<td>SG 17</td>
<td>4-CIC₆H₄</td>
<td>-CH₃</td>
<td>C₁₈H₁₅N₅O₂Cl₂</td>
</tr>
<tr>
<td>SG 18</td>
<td>2-BrC₆H₄</td>
<td>-H</td>
<td>C₁₇H₁₃N₅O₂ClBr</td>
</tr>
<tr>
<td>SG 19</td>
<td>2-OHC₆H₄</td>
<td>-H</td>
<td>C₁₇H₁₄N₅O₃Cl</td>
</tr>
<tr>
<td>SG 20</td>
<td>4-OHC₆H₄</td>
<td>-H</td>
<td>C₁₇H₁₄N₅O₃Cl</td>
</tr>
<tr>
<td>SG 21</td>
<td>2-OHC₆H₄</td>
<td>-CH₃</td>
<td>C₁₈H₁₆N₅O₃Cl</td>
</tr>
<tr>
<td>SG 22</td>
<td>4-OHC₆H₄</td>
<td>-CH₃</td>
<td>C₁₈H₁₆N₅O₃Cl</td>
</tr>
</tbody>
</table>
CHAPTER 4:

This chapter has been divided into two sections 4.1 and 4.2 respectively.

SECTION 4.1:

Series 3: Synthesis and characterization of $N^1$-[α-(substituted aryldenehydrazino)-acyl]-1H-indole, SG 23-34.

Synthetic Procedure: A brief description of the synthesis of compounds is given below:

Equimolar solution of 1H-indole and chloroacetyl chloride in the presence of triethyl amine in dioxane was refluxed on a water bath to give $N^1$-chloroacetyl-1H-indole compound SG 23. The compound SG 23 was reacted with hydrazine hydrate to produce $N^1$-(Hydrazinoacetyl)-1H-indole, compound SG 24. The compound SG 24 on condensation with various carbonyls (TABLE - 3) afforded compounds SG 25-34 (Scheme 3)

Characterization of the compounds SG 23-34: The synthesized compounds SG 23-34 were characterized by chromatographic methods, elemental analysis and spectral data. The melting points of compounds SG 23-34 were determined by open capillary method.

The following structures have been drawn for the synthesised compounds SG 25-34.
Scheme-3

\[ \text{H} \quad \text{CICOCH}_2\text{Cl} \]

\[ \text{H} \quad \text{COCH}_2\text{Cl} \quad \text{SG 23} \quad \text{NH}_2\text{NH}_2 \]

\[ \text{N} \quad \text{COCH}_2\text{NHNH}_2 \quad \text{SG 24} \quad \text{O}\text{=C} \quad \text{R} \quad \text{C} \quad \text{Ar} \]

\[ \text{N} \quad \text{COCH}_2\text{NHN} \quad \text{SG 25-34} \quad \text{CICOCH}_2\text{Cl} \]

\[ \text{N} \quad \text{COCH}_2\text{NH} \quad \text{SG 35-44} \]

The diagram shows a step-by-step chemical reaction process involving the transformation of various chemical structures, including the addition of functional groups and the formation of new bonds.
TABLE-3

<table>
<thead>
<tr>
<th>Compound</th>
<th>Ar</th>
<th>R</th>
<th>Molecular formula</th>
</tr>
</thead>
<tbody>
<tr>
<td>SG 25</td>
<td>-C₆H₅</td>
<td>-H</td>
<td>C₁₇H₁₅N₃O</td>
</tr>
<tr>
<td>SG 26</td>
<td>2-ClC₆H₄</td>
<td>-H</td>
<td>C₁₇H₁₄N₃OCl</td>
</tr>
<tr>
<td>SG 27</td>
<td>4-ClC₆H₄</td>
<td>-H</td>
<td>C₁₇H₁₅N₃OCl</td>
</tr>
<tr>
<td>SG 28</td>
<td>2-ClC₆H₄</td>
<td>-CH₃</td>
<td>C₁₈H₁₆N₃OCl</td>
</tr>
<tr>
<td>SG 29</td>
<td>4-ClC₆H₄</td>
<td>-CH₃</td>
<td>C₁₈H₁₆N₃OCl</td>
</tr>
<tr>
<td>SG 30</td>
<td>2-BrC₆H₄</td>
<td>-H</td>
<td>C₁₇H₁₄N₃OBr</td>
</tr>
<tr>
<td>SG 31</td>
<td>2-OHC₆H₄</td>
<td>-H</td>
<td>C₁₇H₁₅N₃O₂</td>
</tr>
<tr>
<td>SG 32</td>
<td>4-OHC₆H₄</td>
<td>-H</td>
<td>C₁₇H₁₅N₃O₂</td>
</tr>
<tr>
<td>SG 33</td>
<td>2-OHC₆H₄</td>
<td>-CH₃</td>
<td>C₁₈H₁₇N₃O₂</td>
</tr>
<tr>
<td>SG 34</td>
<td>4-OHC₆H₄</td>
<td>-CH₃</td>
<td>C₁₈H₁₇N₃O₂</td>
</tr>
</tbody>
</table>
SECTION 4.2:

Series 4: Synthesis and characterization of N\textsuperscript{1}-[α-(4-substituted aryl-3-chloro-2-oxo-1-azetidinyl amino)-acetyl ]-1H-indole, SG 35-44.

*Synthetic procedure:* The compounds SG 25 - 34 of series 3 on reaction with chloroacetyl chloride in the presence of triethyl amine in dioxane yielded compounds SG 35-44 (*TABLE-4*) (*Scheme-3*)

*Characterization of compounds SG 35-44:* The synthesized compounds SG 35 - 44 were characterized by chromatographic methods, elemental analysis and spectral data. The melting points of compound SG 35-44 were determined by open capillary method.

The following structures have been drawn for the synthesised compounds SG 35-44.
**TABLE-4**

<table>
<thead>
<tr>
<th>Compounds</th>
<th>Ar</th>
<th>R</th>
<th>Molecular formula</th>
</tr>
</thead>
<tbody>
<tr>
<td>SG 35</td>
<td>-C₆H₅</td>
<td>-H</td>
<td>C₁₉H₁₆N₂O₂Cl</td>
</tr>
<tr>
<td>SG 36</td>
<td>2-CIC₆H₄</td>
<td>-H</td>
<td>C₁₉H₁₅N₃O₂Cl₂</td>
</tr>
<tr>
<td>SG 37</td>
<td>4-CIC₆H₄</td>
<td>-H</td>
<td>C₁₉H₁₅N₃O₂Cl₂</td>
</tr>
<tr>
<td>SG 38</td>
<td>2-CIC₆H₄</td>
<td>-CH₃</td>
<td>C₂₀H₁₇N₃O₃Cl₂</td>
</tr>
<tr>
<td>SG 39</td>
<td>4-CIC₆H₄</td>
<td>-CH₃</td>
<td>C₂₀H₁₇N₃O₃Cl₂</td>
</tr>
<tr>
<td>SG 40</td>
<td>2-BrC₆H₄</td>
<td>-H</td>
<td>C₁₉H₁₅N₅O₃Cl Br</td>
</tr>
<tr>
<td>SG 41</td>
<td>2-OHCO₆H₄</td>
<td>-H</td>
<td>C₁₉H₁₆N₃O₃Cl</td>
</tr>
<tr>
<td>SG 42</td>
<td>4-OHCO₆H₄</td>
<td>-H</td>
<td>C₁₉H₁₆N₃O₃Cl</td>
</tr>
<tr>
<td>SG 43</td>
<td>2-OHCO₆H₄</td>
<td>-CH₃</td>
<td>C₂₀H₁₉N₃O₃Cl</td>
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<tr>
<td>SG 44</td>
<td>4-OHCO₆H₄</td>
<td>-CH₃</td>
<td>C₂₀H₁₉N₃O₃Cl</td>
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</table>

**CHAPTER-5:**

This chapter is fully devoted to the biological activity such as antibacterial, antifungal, anti-inflammatory and anticonvulsant of the synthesised compounds SG 1 - 44. This chapter has been divided into three sections 5.1, 5.2 and 5.3 respectively.

**SECTION-5.1:** This section deals with general description of the pharmacology and biological activity such as Antibacterial, Antifungal, Antiinflammatory and Anticonvulsant.
SECTION-5.2: This section has been divided into four sub-sections: 5.2.1, 5.2.2, 5.2.3 and 5.2.4 respectively.

SUB-SECTION-5.2.1:

Evaluation of Antibacterial activity: The antibacterial activity of the synthesized compounds SG 1-44 was determined by filter paper disc method against the following selected bacteria:

(i) *Escherchia coli*.

(ii) *Streptococcus aureus*.

(iii) *Shigella flurexeni* and

(iv) *Shigella dysenteriae*.

*Streptomycin* was used as a standard drug for comparison.

SUB-SECTION-5.2.2:

Evaluation of antifungal activity: The antifungal activity of the synthesized compounds SG 1 - 44 was assayed by filter paper disc method against the following selected fungi:

(i) *Aspergillus niger*.

(ii) *Condida albicans*.

(iii) *Crysosporium pannical* and

(iv) *Rizopus oryzae*.

*Griseofulvin* was used as a standard drug for comparison.

SUB-SECTION 5.2.3:

Evaluation of antiinflammatory activity: The antiinflammatory activity was determined by rat paw oedema method of the synthesised
compounds SG 1 - 44 using carrageenan as an antiinflammatory agent. The phenylbutazone was used as a standard drug for comparison.

**SUB-SECTION 5.2.4:**

*Evaluation of anticonvulsant activity:* The synthesised compounds SG 1-44 were screened for their anticonvulsant activity against the pentylentetrazole induced convolution in albino mice of either sex by the method as given in the literature. The standard drug phenobarbitone was used for comparison.

**SECTION 5.3:** This section includes the results and conclusion of the screening of *antibacterial, antifungal, antiinflammatory* and *anticonvulsant* activities. Some of the synthetic products derived form 1,2,3-benzotrizole and 1H-indole nuclei exhibited pronounced biological activity.