Chapter 2

Section 2.1 Application of the selected heteroyis

Section 2.2 Aim and work plan of the research
Section-2.1. Applications of the selected heteroyls

The molecular modification of known pharmacodynamic compounds is a main kind of research in the field of chemotherapy. The structural modification can be carried out by substituting one group(s) by other group(s), adding new group(s), saturating the compound by adding hydrogens or by modifying the acidity or basicity. In each case a complex Structure Activity Relation is obtained. These relations are identical and serve as a guiding factors in mapping the structural features of the compounds with analogous activities.

A brief description regarding the applications of the heterocyclic moieties, (phenothiazine, benzotriazole, thiadiazole and azetidinone) present in the final compounds has been made herein to explain the suitability and importance of the proposed research work.

PHENOOTHIAZINES

Phenothiazine derivatives exhibit significant antitumor\textsuperscript{13}, antiinflammatory\textsuperscript{14,15}, antimalarial\textsuperscript{16}, anthelmintic\textsuperscript{17}, tuberculostatic\textsuperscript{18}, antipsychotic\textsuperscript{19-21}, anaesthetic\textsuperscript{22}, analgesic\textsuperscript{23}, cardiovascular\textsuperscript{24} and antiparkinsonian\textsuperscript{25,26} activity. Methylene blue (1) is a good dye for cotton due to its fastness to washing, light and chlorine.
Extensive study on phenothiazine and its derivatives show that it has the following types of the pharmacological activity such as (i) antiemetic (ii) anaesthetic (iii) analgesic (iv) sedative (v) tranquilizer (vi) antirefrectory hiccups (vii) antimalarial and (viii) antimicrobial.

Chlorpromazine, 2-chloro-10-(3-diethylaminopropyl) phenothiazine (2) displays an amazing array of physiological actions including gangliolytic, adrenolytic, antifibrillatory, antioedema, antipyretic, anticonvulsant, antisick and antiemetic properties. The manyfold action of this drug has been discussed by Goodman\textsuperscript{27}.

Phenothiazine derivatives of types (3-6) are reported as strong antimicrobial agents\textsuperscript{28-31}. 

\[
\text{Figure 1: Molecular Structure of Phenothiazines} \\
(\text{1}) \\
(\text{CH}_3)_2\text{N} - \text{S} - \text{N(CH}_3)_2 \\
(\text{2}) \\
(\text{CH}_3)_2\text{CN(C}_2\text{H}_5)_2 \text{Cl}
\]
10-(Substituted phenyl hydrozonoacetyl) phenothiazines (7) are reported as good anticonvulsants\textsuperscript{32}. 

\textbf{(7)} \hspace{1cm} \text{Ar = Phenyl, Sub. phenyl.}
2,10-Disubstituted phenothiazines of types (8) and (9) are found to display antiinflammatory activity.

![Chemical structures](image)

Ar=Phenyl, Sub phenyl.

1- (Di-n-butylaminomethyl) - 1/2-phenothiazino-methanolhydrochlorides are reported as antimalarial agents.

10-phenothiazeny carbomethylmethyl-β-10-phenothiazinylpropionate, 2,4,6-trinitrophenoxacyethyl-N-10-phenothiazines are found to exhibit anthelmintic activity.

Perazine, perphenazine and trifluoperazines are reported as neuroleptic and sedative agents whileas 10-(substituted thiazolidinyl) phenothiazines are claimed as antiinflammatory agents.

Phenothiazine derivatives like promethazine (10), promazine (11), chlorpromazine, ethomethazine, and ethopromazine are used as tranquillizer and antihistaminic agents.
$N^{10}$-(N-substituted piperazinoalkyl) phenothiazines of type (12) are claimed as paranoid, sedative and neuroleptic agents\textsuperscript{40,41}.

\begin{align*}
(10) & \\
(11) & \\
(12) & R = \text{alkyl}
\end{align*}

Mecazine pecatal (13) has found its application as psychiatric disorder removing agent and as a tranquilizer\textsuperscript{42,43}.

\begin{align*}
(13) & 
\end{align*}
Some of the phenothiazine derivatives like ahiston and chlorproethazine are found to display antihistaminic, anticonvulsant, antiparkinsonian, antidepressant, antispasmodic, tranquillizer and muscle relaxant activity\textsuperscript{44, 45}.

Phenothiazine of type (14) has reported as a good antidepressant agent\textsuperscript{46}.

\begin{equation}
\text{(14)}
\end{equation}

2-(2-Amino-6-aryl-4-pyrimidinyl) phenothiazines of type (15) and 2-(5-aryl-4,5-dihydro-3-pyrazolyl)-phenothiazines (16) are reported as antiinflammatory agents\textsuperscript{47}.

\begin{equation}
\text{(15)} \quad \text{(16)}
\end{equation}

\textit{Ar} = \text{Phenyl, Sub. phenyl.}
BENZOTRIAZOLES

Benzotriazole has its synthetic value for its numerous applications in industry and agriculture. It has an important place in dyestuffs, optical brighteners, fluorescents, corrosion inhibitors, agrochemicals and photostabilizers.

1-Ethoxy-4-nitrobenzotriazole (17) and 1-methoxy-4-nitrobenzotriazole (18) have been found to display strong herbicidal activity.

![Chemical Structure 17](image)

(17)

![Chemical Structure 18](image)

(18)

Ethyl-2-(5-phenoxy-N1-benzotriazolyl propionate (19) has also exhibited herbicidal activity whereas benzotriazolyl alkanoic acids of type (20) are reported as plant growth promoting agents.

![Chemical Structure 19](image)

(19)

![Chemical Structure 20](image)

(20)

R= Alkyl
Benzotriazole derivative of type (21) is used in whitening of fibres, cellulose acetate and plastics.

\[
\text{CH=CH-} \quad \text{COOH}
\]

(21)

Benzotriazole derivatives are reported as corrosion inhibitors of many metals and alloys including copper, solder, brass, steel, cast iron and aluminium.

Chlorobenzotriazoles are excellent oxidants and chlorinating agents\(^{66}\). On the other hand, 1-hydroxy benzotriazole (22) is used as a co-reagent in peptide-coupling\(^{67}\).

\[
\text{N} \quad \text{N} \\
\text{OH}
\]

(22)

Benzotriazole derivatives have their important place in the therapeutics as a bactericide\(^{68}\), antiinflammatory\(^{69}\), antitumor\(^{70}\), fungicide\(^{71,72}\), antidepressant\(^{73}\), muscle-relaxant\(^{74}\) and antineoplastic\(^{75}\) agent.
Benzotriazole [4,5-d] pyrimidine, 1,2,4-triazolo-1,3,4-thiadiazolobenzotriazoles; 1,2,4-triazolothiadiazynyl benzotriazoles and 1-H-benzotriazole derivatives of types (23) and (24) are reported as potential antimicrobials.

(23)  
(24)

5-And-6-chloro-1-aryyl benzotriazoles of type (25) and (26) are found to display antiinflammatory activity.

(25)  
(26)

N-β-Ribofuranosyl benzotriazole, N-glycynyl benzotriazole, N-β-glucopyranosyl benzotriazole and 4-substituted benzotriazoles of type (27) are also found to display cytostatic activity.
Mannich bases of 5-nitrobenzotriazole of type (28) are reported as potential muscle-relaxant. 2-Substituted benzotriazole derivatives of phenacetin and aspirin are found to exhibit analgesic activity. Benzotriazoles can be successfully applied as human skin protector from uv radiations. 2-(2-Methyl-2-hydroxyphenyl)-benzotriazole of type (29) is used as sun burn-protector.
2,4,6-Trichlorophenoxy acetyl benzotriazole of type (30) and naphthoxy-acetyl \(N^1\)-benzotriazole of type (31) found to display good antiinflammatory activity\(^{82,83}\).

![Chemical Structures](image)

**THIADIAZOLEs**

The -N-C-S-linkage present in thiadiazoles makes them of versatile biological interest as pesticides and chemotherapeutic agents. Thiodiazoles are reported as antibacterial\(^{84-86}\), antifungal\(^{87,88}\), insecticide\(^9\), pesticide\(^{90,91}\), herbicide\(^92\), CNS depressant, sedative, anticonvulsant, antiinflammatory and hypoglycemic agents\(^{93}\).

2,5-Disubstituted-1,3,4-thiadiazoles of type (32) are reported as good antibacterial agents\(^94\).

![Chemical Structure](image)

\(\text{Ar} = \text{Phenyl/Sub. phenyl}\)
2-Arylamino-5-aryloxyethyl-1,3,4-thiadiazoles of type (33) and 2-aryloxy methyl-5-phenyl-1, 3, 4-thiadiazolo [3, 2-a]-1, 3, 5-triazine-7-thiones of type (34) are reported as potential antifungal agents. 

![Chemical Structures](image)

(33)  \( \text{Ph} \)

(34)  \( \text{Ar=Phenyl/Sub.phenyl} \)

2-Substituted-1,3,4-thiadiazolo [2,3-c]-1,2,4-triazino [5,6-b] indoles of type (35) and 3,6,9-triaryl-2-thiothiazolo [4,5-d] [1,3,4] thiaiazolo [2,3-b] pyrimidines are also reported as antifungal agents.

![Chemical Structure](image)

(35)  \( R=\text{H/OH/OCH}_3/\text{CH}_3/\text{Cl} \)

5-[(3-Substituted isoxazolo [4,5-d] pyrimidin-4-yl) oxymethyl]-2-(p-substituted phenyl amino-1,3,4-thiadiazoles and 5-(2’,4’-diphenoxymethyl)-2-(2’-aryl-5’H-4’-thiazolidinone)-1, 3,4-thiadiazoles (36) are found to display antibacterial activity.
2-Amino-5-(4'-hydroxalkoxyl 2',4'-dialkoxy-5'-nitroaryl) - thia-3,4-diazoles of type (37) and 2-anilino-5-[4'-(substituted anilino)] methyl-1,3,4-thiadiazoles of type (38) are found to exhibit antimicrobial activity\textsuperscript{101,102}.

2-(4-Chlorophenoxyethyl)-1,3,4-thiadiazolo [5,1-b]-imidazole-6-ones of type (39) and N-(2-mercapto acetyl)-5-amino (substituted aryl)-1,3,4-thiadiazolyl hydrazines are reported as good pesticides\textsuperscript{103,104}.
2,2-Dialkylphosphate/thiophates of 2-amino-5-(2,4-dichlorophenyl)-1,3,4-thiadiazoles of type (40) are found to act as potential insecticides\textsuperscript{105}.

(40) \hspace{1cm} R=H/CH\textsubscript{3}/C\textsubscript{2}H\textsubscript{5}

2-(Substituted acetyl)-amino-5-alkyl-1,3,4-thiadiazoles of type (41) are reported as CNS depressant\textsuperscript{106}.

(41) \hspace{1cm} R = Acetyl/Sub. acetyl

2-Amino-5-substituted-1,3,4-thiadiazoles of type (42) are found to exhibit CNS depressant, sedative and anticonvulsant activity\textsuperscript{107}.
2-Arylamino-5-[(p-3-aryl-4-oxoquinazolin 3-yl-methylamino) phenyl]-1,3,4-thiadiazoles of type (43) are found to display hypoglycemic activity\textsuperscript{108}.

2-(2-Arylethyl)-5-phenylamino-1,3,4-thiadiazole of type (44) are found to exhibit antiamoebic activity\textsuperscript{109}.
AZETIDINONES

Staudinger\textsuperscript{110} before 1912, initiated work on the chemistry of 2-azetidinones. Interest in these 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 these compounds.

A large number of antibiotics contain azetidinone moiety\textsuperscript{111,112}. The reactivity of azetidinones influences largely on substitution\textsuperscript{113,114}. 2-Azetidinones and its derivatives possess variety of therapeutic activities\textsuperscript{115,116}.

4-Aryl-3-chloro-1-(4-phenyl-2-oxazolyl)-azetidine-2-ones of type (45) and 1''-[4''-aryl (2',4'-bithiazol)-2'-yl]-4''-aryl-2''-azetidinones of type (46) are found to display antibacterial activity\textsuperscript{117,118}.

![Diagram of 2-Azetidinones]

\begin{align*}
\text{(45)}
\end{align*}

\begin{align*}
\text{(46)} \quad X=\text{CH}_3/\text{OCH}_3/\text{NO}_2/\text{Cl}/\text{Br}
\end{align*}

1-[5'-{(Substituted phenoxy methyl)-1,3,4-thiadiazol-2-yl}]-4-substituted-2-azetidinones of type (47) and 1-[5'-aryl-1, 3, 4-thiadiazol-2'-yl]-3-chloro-4-
substituted-2-azetidinones of type (48) are reported as potential antifungal agents$^{119,120}$.

![Molecular Structure](47)

![Molecular Structure](48) \( X = \text{CH}_3/\text{OCH}_3/\text{NO}_2/\text{Cl}/\text{Br} \)

4-Aryl-1-(phenothiazinoamidy)-2-azetidinones of type (49) and 5-aryl-2-[spiro-(1,3-dithiolone)-2,4-(3'-chboro-2'-azetidinon)-1'-yl]-1,3,4-oxa/thiadiazoles of type (50) are found to exhibit antiinflammatory activity$^{121,122}$.

![Molecular Structure](49)

![Molecular Structure](50) \( \text{Ar}=\text{Phenyl/Sub. phenyl} \)
Benzothiazolosulphonamidoazetidin-2-ones (51) are reported to exhibit antimicrobial activity against pathogen *B. subtilis*, *S. aureus*, *E. coli* and *P. aeruginosa*\[^{123}\].

![Chemical structure of 51]

\[X = CH_3/OCH_3/NO_2/Cl/Br\]

1, 3, 7, 9-Tetрабromo - 10 [α-{2-(2-hydroxy phenyl)-3-chloro-4-oxo-1-azetidinylamino}acetyl] phenothiazines of type (52) are found to display tuberculostatic activity\[^{30}\].

![Chemical structure of 52]

\[X = CH_3/OCH_3/OH/NO_2/Cl\]

3-Chloro-2-oxo-4-(substituted phenyl)-azetidin-1-yl-thioureas of type (53) are found to exhibit antiparkinsonian activity\[^{124}\].
Substituted-2-oxo-3-chloro-3-(2-chlorophenoxy)-4-arylindol-3-yl) azetidines of type (54) are reported as CNS depressant and antiinflammatory agents\textsuperscript{125}.

1-[2-Alkyl-4-(3H)-oxo-3-quinazolinyl]-4-aryl-3-chloro-2-azetidinones of type (55) are found to display antiparkinsonian, antitubercular and antirigidity activity\textsuperscript{126}.
Section 2.2 Aim and work plan of the research

The literature survey on structure-activity relationship of phenothiazines, benzotriazoles, thiadiazoles and azetidinones has prompted the author to synthesise some phenothiazinyli thiadiazoles, phenothiazinyli thiadiazolozetidinones, benzotriazolothiadiazoles and benzotriazolylthiadiazolozetidinones and to assay their pharmacological activity such as antibacterial, antifungal, anti-inflammatory, analgesic and anticonvulsant activity to get new compounds as a possible new age drugs.

Work plan of the research:

The work plan of the research has been divided into three parts:

Part-I: Synthesis of new heterocyclic compounds.

Part-II: Characterization of the compounds.

Part-III: Pharmacological activity assessment of the synthesised compounds.

PART-I: Synthesis of the new heterocyclic compounds:

Four series of compounds have been synthesised by following the scheme-1 (Page No. 66).

Series-1: 2-Aryldenylamino-5-(N¹⁰-phenothiazinomethyl)-1,3,4-thiadiazoles:

The compounds of series-1 (compounds 4-14) have been synthesised through the compounds 1-3 by following the first four steps of the scheme -2 (Page No. 67).
Scheme-1

Het\(\text{N} - \text{H}\)
\[\xrightarrow{\text{ClCH}_2\text{COOC}_2\text{H}_5}\]
Het\(\text{N} - \text{CH}_2\text{COOC}_2\text{H}_5\)
\[\xrightarrow{\text{H}_2\text{NNHCSNH}_2}\]
Het\(\text{N} - \text{CH}_2\text{CONHNHCSNH}_2\)
\[\xrightarrow{\text{H}_2\text{SO}_4}\]
Het\(\text{N} - \text{CH}_2\xrightarrow{\text{AcOH} / \xrightarrow{\text{R}_1 > C = O}} \text{C} - \text{NH}_2\)
\[\xrightarrow{\text{R}_2}\]
Het\(\text{N} - \text{CH}_2\xrightarrow{\text{CIC} = \text{CON} / \text{Et}_3\text{N}} \text{C} - \text{N} = \text{C}_1\)
\[\xrightarrow{\text{R}_1 \text{C}_2}\]
Het\(\text{N} - \text{CH}_2\xrightarrow{\text{ClCH}_2\text{COCl} / \text{Et}_3\text{N}} \text{C} - \text{S} - \text{C} - \text{N} - \text{C}_1\)
\[\xrightarrow{\text{R}_1 \text{C}_2}\]

Where: Het\(\text{N} - \text{H}\) = Heterocycle (phenothiazine / benzotriazole) \(R_1 = R_2 = \text{H} / \text{CH}_3 / \text{aryl} / \text{sub.aryl}\)
Scheme 2

\[
\begin{align*}
 &\text{N} \\
 &\text{S} \\
 &\text{CICH}_2\text{COOC}_2\text{H}_5 \\
 &\text{H}_2\text{NNHCSNH}_2 \\
 &\text{CH}_2\text{CONNHCSNH}_2 \\
 &\text{H}_2\text{SO}_4 \\
 &\text{N} \quad \text{N} \quad \text{C} \quad \text{S} \quad \text{C} \quad \text{NH}_2 \\
 &\text{O} = \text{C} \quad \text{R}_1 \\
 &\text{CICH}_2\text{COCl} / \text{Et}_3\text{N} \\
 &\text{N} \quad \text{N} \quad \text{C} \quad \text{S} \quad \text{C} \quad \text{N} = \text{C} \quad \text{R}_2 \\
 &\text{CH}_2 \\
 &\text{Where } R_1 = R_2 = \text{H} / \text{CH}_3 / \text{aryl} / \text{sub-aryl}
\end{align*}
\]
<table>
<thead>
<tr>
<th>Compounds No.</th>
<th>Chemical Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>2-Benzylidenylamino-5-(N\textsuperscript{10}-phenothiazinomethyl)-</td>
</tr>
<tr>
<td></td>
<td>1,3,4-thiadiazole.</td>
</tr>
<tr>
<td>5</td>
<td>2-(4-Methoxy benzylidenylamino)-5-(N\textsuperscript{10}-phenothiazinomethyl)-</td>
</tr>
<tr>
<td></td>
<td>1,3,4-thiadiazole.</td>
</tr>
<tr>
<td>6</td>
<td>2-Cinnamylidenylamino-5-(N\textsuperscript{10}-phenothiazinomethyl)-1,3,4-</td>
</tr>
<tr>
<td></td>
<td>thiadiazole.</td>
</tr>
<tr>
<td>7</td>
<td>2-(2-Chlorobenzylidenylamino)-5-(N\textsuperscript{10}-phenothiazinomethyl)-</td>
</tr>
<tr>
<td></td>
<td>1,3,4-thiadiazole.</td>
</tr>
<tr>
<td>8</td>
<td>2-(4-Chlorobenzylidenylamino)-5-(N\textsuperscript{10}-phenothiazinomethyl)-</td>
</tr>
<tr>
<td></td>
<td>1,3,4-thiadiazole.</td>
</tr>
<tr>
<td>9</td>
<td>2-(4-Dimethylaminobenzylidenylamino)-5-(N\textsuperscript{10}-</td>
</tr>
<tr>
<td></td>
<td>phenothiazinomethyl)-1,3,4-thiadiazole.</td>
</tr>
<tr>
<td>10</td>
<td>2-Furfurylidenylamino-5-(N\textsuperscript{10}-phenothiazinomethyl)-1,3,4-</td>
</tr>
<tr>
<td></td>
<td>thiadiazole.</td>
</tr>
<tr>
<td>11</td>
<td>2-(2-Hydroxybenzylidenylamino)-5-(N\textsuperscript{10}-phenothiazinomethyl)-</td>
</tr>
<tr>
<td></td>
<td>1,3,4-thiadiazole.</td>
</tr>
<tr>
<td>12</td>
<td>2-(α-Methylbenzylidenylamino)-5-(N\textsuperscript{10}-phenothiazinomethyl)-</td>
</tr>
<tr>
<td></td>
<td>1,3,4-thiadiazole.</td>
</tr>
<tr>
<td>13</td>
<td>2-(α-Methyl-2-hydroxybenzylidenylamino)-5-(N\textsuperscript{10}-</td>
</tr>
<tr>
<td></td>
<td>phenothiazinomethyl)-1,3,4-thiadiazole.</td>
</tr>
<tr>
<td>14</td>
<td>2-(α-Phenylbenzylidenylamino)-5-(N\textsuperscript{10}-phenothiazinomethyl)-</td>
</tr>
<tr>
<td></td>
<td>1,3,4-thiadiazole.</td>
</tr>
</tbody>
</table>
Series-2 : N^{10}-Phenothiazinomethyl thiadiazoloazetidinones :

The compounds of series-2 (compounds 15-25) have been synthesised using compounds of series-1 as precursor and by following the last step of the scheme-2 (Page No. 67).

**Table-2.2: List of the compounds synthesised under series-2**

<table>
<thead>
<tr>
<th>Compounds No.</th>
<th>Chemical Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>15. 1-[5’-(N^{10}-Phenothiazinomethyl)-1’,3’,4’-thiadiazol-2’-yl]-4-phenyl-3-chloro-2-oxo-azetidine.</td>
<td></td>
</tr>
<tr>
<td>16. 1-[5’-(N^{10}-Phenothiazinomethyl)-1’,3’,4’-thiadiazol-2’-yl]-4-(4-methoxyphenyl)-3-chloro-2-oxo-azetidine.</td>
<td></td>
</tr>
<tr>
<td>17. 1-[5’-(N^{10}-Phenothiazinomethyl)-1’,3’,4’-thiadiazol-2’-yl]-4-(2-phenyl ethenyl)-3-chloro-2-oxo-azetidine.</td>
<td></td>
</tr>
<tr>
<td>18. 1-[5’-(N^{10}-Phenothiazinomethyl)-1’,3’,4’-thiadiazol-2’-yl]-4-(2-chlorophenyl)-3-chloro-2-oxo-azetidine.</td>
<td></td>
</tr>
<tr>
<td>19. 1-[5’-(N^{10}-Phenothiazinomethyl)-1’,3’,4’-thiadiazol-2’-yl]-4-(4-chlorophenyl)-3-chloro-2-oxo-azetidine.</td>
<td></td>
</tr>
<tr>
<td>20. 1-[5’-(N^{10}-Phenothiazinomethyl)-1’,3’,4’-thiadiazol-2’-yl]-4-(4-dimethylaminophenyl)-3-chloro-2-oxo-azetidine.</td>
<td></td>
</tr>
<tr>
<td>22. 1-[5’-(N^{10}-Phenothiazinomethyl)-1’,3’,4’-thiadiazol-2’-yl]-4-(2-hydroxyphenyl)-3-chloro-2-oxo-azetidine.</td>
<td></td>
</tr>
<tr>
<td>23. 1-[5’-(N^{10}-Phenothiazinomethyl)-1’,3’,4’-thiadiazol-2’-yl]-4-methyl-4-phenyl-3-chloro-2-oxo-azetidine.</td>
<td></td>
</tr>
<tr>
<td>24. 1-[5’-(N^{10}-Phenothiazinomethyl)-1’,3’,4’-thiadiazol-2’-yl]-4-methyl-4-(2-hydroxyphenyl)-3-chloro-2-oxo-azetidine.</td>
<td></td>
</tr>
<tr>
<td>25. 1-[5’-(N^{10}-Phenothiazinomethyl)-1’,3’,4’-thiadiazol-2’-yl]-4,4-diphenyl-3-chloro-2-oxo-azetidine.</td>
<td></td>
</tr>
</tbody>
</table>
Series-3: 2-Arylidenylamino-5-benzotriazolomethyl-1,3,4-thiadiazoles:

The compounds of series-3-(compound 29-39) have been prepared through the compounds 26-28 by following the first four steps of scheme-3 (Page No.72).

**Table-2.3: List of the compounds synthesised under series-3**

<table>
<thead>
<tr>
<th>Compounds No.</th>
<th>Chemical Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>29.</td>
<td>2-Benzylidenylamino-5-(N&lt;sub&gt;1&lt;/sub&gt;-benzotriazolo-1,3,4-thiadiazole</td>
</tr>
<tr>
<td>30.</td>
<td>2-(4-Methoxybenzylidenylamino-5-(N&lt;sub&gt;1&lt;/sub&gt;-benzotriazolomethyl)-1,3,4-thiadiazole</td>
</tr>
<tr>
<td>31.</td>
<td>2-Cinnamylidenylamino-5-(N&lt;sub&gt;1&lt;/sub&gt;-benzotriazolomethyl)-1,3,4-thiadiazole</td>
</tr>
<tr>
<td>32.</td>
<td>2-(2-Chlorobenzylidenylamino-5-(N&lt;sub&gt;1&lt;/sub&gt;-benzotriazolomethyl)-1,3,4-thiadiazole</td>
</tr>
<tr>
<td>33.</td>
<td>2-(4-Chlorobenzylidenylamino-5-(N&lt;sub&gt;1&lt;/sub&gt;-benzotriazolomethyl)-1,3,4-thiadiazole</td>
</tr>
<tr>
<td>34.</td>
<td>2-(4-Dimethylaminobenzylidenylamino-5-(N&lt;sub&gt;1&lt;/sub&gt;-benzotriazolomethyl)-1,3,4-thiadiazole</td>
</tr>
<tr>
<td>35.</td>
<td>2-Furfurylidenylamino-5-(N&lt;sub&gt;1&lt;/sub&gt;-benzotriazolomethyl)-1,3,4-thiadiazole</td>
</tr>
<tr>
<td>36.</td>
<td>2-(2-Hydroxybenzylidenylamino-5-(N&lt;sub&gt;1&lt;/sub&gt;-benzotriazolomethyl)-1,3,4-thiadiazole</td>
</tr>
<tr>
<td>37.</td>
<td>2-(α-Methylbenzylidenylamino-5-(N&lt;sub&gt;1&lt;/sub&gt;-benzotriazolomethyl)-1,3,4-thiadiazole</td>
</tr>
<tr>
<td>38.</td>
<td>2-(α-Methyl-2-hydroxybenzylidenylamino-5-(N&lt;sub&gt;1&lt;/sub&gt;-benzotriazolomethyl)-1,3,4-thiadiazole</td>
</tr>
<tr>
<td>39.</td>
<td>2-(α-Phenylbenzylidenylamino-5-(N&lt;sub&gt;1&lt;/sub&gt;-benzotriazolo methyl)-1,3,4-thiadiazole</td>
</tr>
</tbody>
</table>
Series-4: N\textsuperscript{1}-benzotriazolomethyl thiadiazolo azetidinones:

The compounds of series-4 (compounds 40-50) have been synthesised using the compounds of series-3 as a precursor and by following the last step of the scheme-3 (Page No. 72).

**Table-2.4: List of the compounds synthesised under series -4**

<table>
<thead>
<tr>
<th>Compound No.</th>
<th>Chemical Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>40.</td>
<td>(1-[\text{5'-(N}^1\text{-benzotriazolomethyl)-1',3',4'-thiadiazol-2'-yl]}-4\text{-phenyl-3-chloro-2-oxo azetidine.} )</td>
</tr>
<tr>
<td>41.</td>
<td>(1-[\text{5'-(N}^1\text{-benzotriazolomethyl)-1',3',4'-thiadiazol-2'-yl]}-4\text{- (4-methoxyphenyl)-3-chloro-2-oxo azetidine.} )</td>
</tr>
<tr>
<td>42.</td>
<td>(1-[\text{5'-(N}^1\text{-benzotriazolomethyl)-1',3',4'-thiadiazol-2'-yl]}-4\text{- (2-phenyl ethenyl)-3-chloro-2-oxo azetidine.} )</td>
</tr>
<tr>
<td>43.</td>
<td>(1-[\text{5'-(N}^1\text{-benzotriazolomethyl-1',3',4'-thiadiazol-2'-yl]}-4\text{- (2-chlorophenyl)-3-chloro-2-oxo azetidine.} )</td>
</tr>
<tr>
<td>44.</td>
<td>(1-[\text{5'-(N}^1\text{-benzotriazolomethyl-1',3',4'-thiadiazol-2'-yl]}-4\text{- (4-chlorophenyl)-3-chloro-2-oxo azetidine.} )</td>
</tr>
<tr>
<td>45.</td>
<td>(1-[\text{5'-(N}^1\text{-benzotriazolomethyl-1',3',4'-thiadiazol-2'-yl]}-4\text{- (dimethylaminophenyl)-3-chloro-2-oxo azetidine.} )</td>
</tr>
<tr>
<td>46.</td>
<td>(1-[\text{5'-(N}^1\text{-benzotriazolomethyl-1',3',4'-thiadiazol-2'-yl]}-4\text{- (2-furyl)-3-chloro-2-oxo azetidine.} )</td>
</tr>
<tr>
<td>47.</td>
<td>(1-[\text{5'-(N}^1\text{-benzotriazolomethyl-1',3',4'-thiadiazol-2'-yl]}-4\text{- (2-hydroxyphenyl)-3-chloro-2-oxo azetidine.} )</td>
</tr>
<tr>
<td>48.</td>
<td>(1-[\text{5'-(N}^1\text{-benzotriazolomethyl-1',3',4'-thiadiazol-2'-yl]}-4\text{-methyl-4-phenyl-3-chloro-2-oxo azetidine.} )</td>
</tr>
<tr>
<td>49.</td>
<td>(1-[\text{5'-(N}^1\text{-benzotriazolomethyl-1',3',4'-thiadiazol-2'-yl]}-4\text{-methyl-4-(2-hydroxyphenyl)-3-chloro-2-oxo-azetidine.} )</td>
</tr>
<tr>
<td>50.</td>
<td>(1-[\text{5'-(N}^1\text{-benzotriazolomethyl-1',3',4'-thiadiazol-2'-yl]}-4,4\text{-diphenyl-3-chloro-2-oxo azetidine.} )</td>
</tr>
</tbody>
</table>
Scheme 3

Where: $R_1 = R_2 = H / CH_3 / aryl / sub. aryl$
PART-II : Characterization of the synthesised compounds :

The melting points of the compounds have been determined in an open capillary and are uncorrected. Rf values were determined by TLC on silica gel coated plates using iodine as a developer. All the compounds were analysed for C, H and N percentage. The IR spectra of the representative compounds were recorded in KBr palletes on Acculab-10-spectrophotometer and $^1$H-NMR spectra of the representative compounds were recorded on Perking-Elmer R-32 spectrometer at 90 MHz using TMS as an internal standard.

PART-III : Pharmacological activity assessment of the synthesised compounds :

The synthesised compounds were screened for their antibacterial, antifungal, antiinflammatory, analgesic and anticonvulsant activities. Some of the compounds were found to display remarkable pharmacological activity.