3.1. INTRODUCTION

A diversity of useful biological effects is possessed by tetrahydroimidazole (imidazolidine) nucleus. There are many examples of this nucleus containing drugs (Table 3.1).

Table 3.1: Imidazolidines or related nucleus containing drugs:

<table>
<thead>
<tr>
<th>Name</th>
<th>Structure</th>
<th>Medicinal Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anagrelide</td>
<td><img src="image" alt="Structure of Anagrelide" /></td>
<td>Antithrombotic Agents; Fibrinolytic Agents</td>
</tr>
<tr>
<td>Azlocillin</td>
<td><img src="image" alt="Structure of Azlocillin" /></td>
<td>Anti-bacterial Agents</td>
</tr>
<tr>
<td>Dantrolene</td>
<td><img src="image" alt="Structure of Dantrolene" /></td>
<td>Muscle Relaxants</td>
</tr>
<tr>
<td>Ethotoin</td>
<td><img src="image" alt="Structure of Ethotoin" /></td>
<td>Anticonvulsants</td>
</tr>
<tr>
<td>Clonidine</td>
<td><img src="image" alt="Structure of Clonidine" /></td>
<td>Antihypertensive</td>
</tr>
<tr>
<td>Fentuconazole</td>
<td><img src="image" alt="Structure of Fentuconazole" /></td>
<td>Antifungal Agents</td>
</tr>
</tbody>
</table>
### Pantoprazole
- **Structure:** ![Pantoprazole Structure](image)
- **Category:** Antiulcer Agents

### Nilutamidhe
- **Structure:** ![Nilutamide Structure](image)
- **Category:** Anticancer Agents

### Flutrimazole
- **Structure:** ![Flutrimazole Structure](image)
- **Category:** Antifungal

### Naphazoline
- **Structure:** ![Naphazoline Structure](image)
- **Category:** Nasal decongestant

### Decarbazine
- **Structure:** ![Decarbazine Structure](image)
- **Category:** Antineoplastic agent

### Imidapril
- **Structure:** ![Imidapril Structure](image)
- **Category:** Antihypertensive

### Antazoline
- **Structure:** ![Antazoline Structure](image)
- **Category:** Antihistaminic
Tetrahydroimidazole ring system itself is primary molecular scaffold upon which characteristic pharmacophore for various receptors can be assembled (Mulwad, et al., 2011; Kanagarajan, et al., 2011). 1,2,3-Trisubstituted tetrahydroimidazoles of following general structure are reported to have good anti-inflammatory and antimicrobial activities (Perillo, et al., 2005; Khan, et al., 2002; Sharma, et al., 2001).

\[
\begin{array}{c}
\text{NN} \\
\text{R} \\
\text{R}_1 \\
\text{R}
\end{array}
\]

Similarly, naphthalene nucleus plays significant role in drug design. There are reports that incorporation of naphthalene nucleus in a compound increases its biological activity (Upadhayaya, et al., 2010; Vargas, et al., 2008). This nucleus is reported to have numerous biological activities (Ono, et al., 1999; Rokade, et al., 2009).

During literature survey it was found that compounds containing two naphthalene rings and some heterocyclic nucleus in the same framework have medicinal value. Examples are mentioned in Table 3.2. Many naphthalene nucleus containing drugs are also available in the market (Table 3.2) and play a vital role as promising clinical agents (Gonzalo-Garijo, et al., 2007; Dannhardt, et al., 2001; Wright, et al., 1999; White, et al., 1998; Mak, 2004).
### Table 3.2: Examples of naphthalene ring containing drugs/compounds

<table>
<thead>
<tr>
<th>Name</th>
<th>Structure</th>
<th>Medicinal Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nabumetone;</td>
<td>4-(6-methoxynaphthalen-2-yl)butan-2-one</td>
<td>Anti-inflammatory Agent</td>
</tr>
<tr>
<td>Naproxen</td>
<td>(2S)-2-(6-methoxynaphthalen-2-yl)propanoic acid</td>
<td>Anti-inflammatory Agent</td>
</tr>
<tr>
<td>Nafcillin;</td>
<td>(2S,5R,6R)-6-(2-ethoxy-naphthalene-1-amido)-3,3-dimethyl-7-oxo-4-thio-1-azabicyclo-[3.2.0]heptane-2-carboxylic acid</td>
<td>Anti-bacterial Agent</td>
</tr>
<tr>
<td>Naftifine;</td>
<td>methyl(naphthalen-1-ylmethyl)(3-phenylprop-2-en-1-yl)amine</td>
<td>Antifungal Agent</td>
</tr>
<tr>
<td>Tolnaftate;</td>
<td>N-methyl-N-(3-methylphenyl)-1-(naphthalen-2-yloxy)methanethioamide</td>
<td>Antifungal Agent</td>
</tr>
<tr>
<td>Terbinafine;</td>
<td>(6,6-dimethylhept-2-en-4-yn-1-yl) (methyl) (naphthalen-1-ylmethyl) amine</td>
<td>Enzyme Inhibitor</td>
</tr>
<tr>
<td>Cinacalcet;</td>
<td>[(1R)-1-(naphthalen-1-yl)ethyl][3-[3-(trifluoromethyl)phenyl]propyl] amine</td>
<td>Calcimimetics</td>
</tr>
</tbody>
</table>
### Suramin;

8-[(4-methyl-3-[[3-((2-methyl-5-((4,6,8-trisulfonaphthalen-1-yl)carbamoyl)phenyl)carbamoyl)phenyl]carbamoyl)amino]benzene]amido]benzene-1,3,5-trisulfonic acid

![Structure](image)

(This structure contains two naphthalene rings)

- Antineoplastic Agent;
- Trypanocidal Agent

### Propranolol;

[2-hydroxy-3-[(naphthalen-1-yloxy)propyl](propan-2-yl)amine

![Structure](image)

- Anti-anxiety Agent;
- Antihypertensive Agent.

1-[[((2-hydroxy-1-naphthyl)methyl][(substituted)amino]methyl]-2-naphthol (Huang et al., 2003)

![Structure](image)

(This structure contains two naphthalene rings)

- Antinflammatory activity

3,5-dinaphthalene-1-yls-substituted-2-pyrazolines (Azarifar, et al., 2002)

![Structure](image)

(This structure contains two naphthalene rings and heterocyclic nucleus)

- Antimicrobial activity

### Adapalene;

6-[3-(adamantan-1-yl)-4-methoxyphenyl]naphtalen-2-carboxylic acid

![Structure](image)

- Dermatologic agent

Based on the above literature it was planned to incorporate naphthalene nucleus in tetrahydroimidazoles with aim of getting compounds of good anti-inflammatory and antimicrobial activities.