PART - A

CHAPTER - 1

INTRODUCTION
Chapter-1

Oxygen heterocycle--furan, due to its wide spectrum of physiological and pharmacological properties, has captured interest of chemists all over the world especially in recent years. The compounds encompassing furan nucleus are widely distributed in nature especially among the plant kingdom. Thus, synthesis of furan and the compounds encompassing furan has been explored to maximum extent over the past century. This has resulted in more selective and versatile approaches for the synthesis of such compounds1.

Benzofuran which is formed by the fusion of benzene nucleus with furan moiety has also been found to be associated with important biological activities. The compounds of benzofuran are not common in nature. However, several synthetic derivatives of benzofuran have been prepared and found to possess wide range of pharmacological activities.

On condensation with naphthalene nucleus, furan gives yet another heterocyclic compound naphthofuran.

Although, all these oxygen heterocycles, furan, benzofuran and naphthofuran are rarely found in nature, their importance has been revealed when such isolated compounds were evaluated for various biological and pharmacological activities. Hence, synthetic organic chemists have directed the research work towards the synthesis of derivatives of these heterocycles with aim to obtain more potent molecules having enhanced biological profile with minimum side effects. The results of such investigations are summarized briefly in the following pages, which also justifies the aim of the present research work.
1. Compounds containing furan nucleus

Furan 1 is the five membered ring containing oxygen as heteroatom. It is frequently found associated with other oxygen heterocycles such as α-pyran and γ-pyran in nature\textsuperscript{2-7}. It’s nitro derivative, 2-nitrofuran, 2 is widely used as antibacterial and anti parasitic agent.

![Furan structures](image)

Encouraged by these observations, series of nitro derivatives of furan have been synthesized, amongst which nitrofurantoin and nitrofuroxazide are the best known antibacterial agents\textsuperscript{8}. The antibacterial effect of such compounds has been attributed to metabolic activation through the reduction of nitro group\textsuperscript{9}. Recently Tangallapally reported the synthesis of 5-nitrofuran-2-carboxylicacid-4(4-benzyl-piperazin-1-yl) benzylamide with improved antitubercular property\textsuperscript{10}.

Polyhydroxylated piperidines\textsuperscript{11} such as (+)-desoxoprosophylline\textsuperscript{12} and (+)-6-epicostanospermine\textsuperscript{13} have been synthesized by using 2-amino-2-(2-furyl)ethan-1-ol as an intermediate which in term was obtained by reduction of corresponding nitro compound. Chen \textit{et al} reported synthesis of some derivatives of 2-(furan-2-yl)-4-(phenoxy)quinolines which exhibited considerable cytotoxicity and antiinflammatory properties\textsuperscript{14}.

Furans with basic side chains are novel series of antagonists with selectivity for the estrogen receptor alpha in terms of binding affinity and potency of transcriptional activation\textsuperscript{15}.

There are several synthetic routes available in literature for the formation of furan nucleus and its derivatives\textsuperscript{16-21}. 
Lee et al., could achieve one pot synthesis of 2-phenyl-5-phthalamidefuran 3 by reacting benzyl chloride and phenyl propargyl ether, minimising reaction time and obtaining high yield\textsuperscript{22}.

![Structure of 3]

2. Compounds containing benzofuran nucleus

Benzofuran 4 formed by the condensation of benzene ring and furan nucleus is found less common in nature. However, numerous benzofuran derivatives have been synthesised and several of them have been found to possess wide range of biological and pharmacological activities such as antimicrobial\textsuperscript{23-24}, antiviral\textsuperscript{25}, analgesic\textsuperscript{26}, anti inflammatory\textsuperscript{27} and antidiabetic\textsuperscript{28}.

![Structure of 4]

The development of chemistry of benzofurans is of significant importance as it is analogous to indole and benzothiophene. However, the chemistry of benzofurans is relatively less explored when compared to those of indole and benzothiophene. The research work in this area was initially aimed at the isolation of biologically active products possessing furans and benzofuran ring systems. Thereafter, the attention was shifted to the structural modification of natural products, in order to improve efficacy and to minimize
toxicity. Such type of research work has resulted in accumulation of voluminous literature and several monographs devoted to the study of both natural and synthetic benzofurans have appeared in literature\textsuperscript{29-33}.

The detailed discussion about the investigation of benzofuran is out of scope of this thesis, hence only a few important research findings have been summarised in the following pages.

2.1 Naturally occurring benzofuran compounds

2.1.1 Benzofuran fused with oxygen heterocycles

Benzofuran compounds exist in great structural variety and in large number in nature. The following compounds have been shown to exhibit important biological activities which are conveniently grouped, based upon their chemical structure.

a. Simple benzofurans

\[
\begin{align*}
\text{H}_3\text{CO} & \quad \text{C}_2\text{H}_5 \\
\text{OCH}_3 & \quad \text{C}_6\text{H}_5
\end{align*}
\]

2-Ethyl-5-methoxy-1-benzofuran\textsuperscript{34}

\[
\begin{align*}
\text{CH}_3 & \quad \text{CH}_3 \\
\text{OCH}_3 & \quad \text{C}_6\text{H}_5
\end{align*}
\]

Tremetone\textsuperscript{35}

\[
\begin{align*}
\text{OCH}_3 & \quad \text{C}_6\text{H}_5
\end{align*}
\]

Pongamol\textsuperscript{36}
b. Dibenzofurans

![Usnic Acid](image)

Usnic Acid\textsuperscript{37}

c. β-Coumaranones

![Griseofulvin](image)

Griseofulvin\textsuperscript{38}

d. α-Pyranobenzofuran (Furocoumarins)

![Psoralen](image)

Psoralen\textsuperscript{39}

![Visnagin](image)

Visnagin\textsuperscript{40-43}

e. γ-Pyranobenzofurans

i. Furochromones

![Karanjin](image)

Karanjin\textsuperscript{44}
ii. Furoflavones

![Neotenone](image)

iii. Furoisoflavones

![6-Methylsterigmatocystin](image)

iv. Furoxanthones

![Pterocarpin](image)

v. Furoflavonoids and Rotenoids:

![Elliptone](image)
2.1.2. Benzofuran fused with nitrogen heterocycle

Benzofuran nucleus is very rarely found in combination with nitrogen heterocycles in natural products. Dihydrobenzofuran moiety is found to constitute the part of the structure of opium alkaloids along with other nitrogen heterocyclic systems. The opium alkaloids which are well known for their analgesic activity since ancient times are known to contain morphine 5 and related alkaloids, such as heroin 6 and codeine as their active principles.\(^5\)

\[
\begin{align*}
\text{Morphine} & \quad 5 \\
\text{Heroin} & \quad 6
\end{align*}
\]

Several derivatives of morphine such as morphine sulphate, diamorphine hydrochloride etc. possess potent narcotic and analgesic properties and are used in clinical practice.\(^5\)

Structure activity relationship studies of morphine have been extensively investigated by Small \textit{et al.,}\(^5\) After enormous work, they could find some interesting correlation between physiological activity and structure. They observed that cleavage of ether bridge (dihydrofuran ring) decreases the activity to considerable extent.

Hence, furan moiety plays significant role in imparting analgesic activity to morphine and its related alkaloids.
Another interesting alkaloid, galanthamine, isolated from haemanthus and galanthus, contains dihydrobenzofuran nucleus along with seven membered nitrogen heterocycle. Galanthamine is known to inhibit cholinesterase activity in animals particularly in brain and blood and also shown to exhibit strong bactericidal properties. Hence, this alkaloid finds applications in the treatment of thrombosis, hemiplegics and hemiparetis with cerebral hemorrhage. Intravenous administration of galanthamine results in fall in blood pressure with simultaneous increases in tonus and peristalsis of intestine in cats and rabbits.

Furoquinoline alkaloids represent another class of naturally occurring compounds containing furan moiety. Many of these are reported to possess toxic properties. The exact study of their pharmacological activity was difficult to carry out, due to high insoluble nature of free bases and very high acidity of their salts in aqueous solution.

Typical compounds belonging to this groups are dictamine, skimmianine and acronycidine.

2.2 Synthetic benzofuran compounds

Various methods have been reported in literature for the synthesis of substituted benzofurans. By using α-(methylsulfanyl)ketones and 4-chlorophenol, Kim et al., synthesised 2-alkylbenzofuran 7 derivatives.
Similarly, 2,3-dimethylbenzofuran 8 was synthesised from phenol using 3-chloro-3(methyl)thio-2-butanone in presence of stannous chloride using dichloromethane as solvent. Microwave irradiation to drive the condensation of α-tosyloxyketones with derivatives of salicylaldehyde on potassium fluoride doped alumina was achieved to obtain 2-aryl benzofurans. An interesting conversion of benzothiophene, which is one of the constituents of the diesel oil, to benzofuran was accomplished by bio-disulfurization in presence of *Rhodococcus* species.

2.2.1 Synthetic benzofuran compounds fused with nitrogen heterocycles

Nitrogen heterocycles fused with benzofuran in nature are very much limited. However, due to their important and valuable medicinal properties have been boost for the synthesis of this rare class of compounds. The fact that, furan ring plays vital role in these
compounds for their medicinal properties, has further generated lot of interest in the synthesis of compounds containing benzofuran condensed with other nitrogen heterocycles.

The nitrogen heterocycles can be combined with benzofuran nucleus in different ways. The two ring systems may be condensed together or ring systems may be linked directly with each other to form biheterocycles or through nitrogen or carbon bridge.

The literature survey revealed that, various nitrogen heterocycles starting from three membered ring to seven membered ring have been synthesized by various organic chemists, with different purposes. Jones et al reported the synthesis of benzofuro[2,3-b]azirine 9 in the form of an adduct obtained by the addition of phthalimidonitrine to benzofuran.\textsuperscript{74-75} There is only one report concerning the fusion of 4-membered nitrogen heterocycle with benzofuran due to Christian, who reported the formation of 2,7-dihydro benzofuro[2,3-b]azete 10 during the photolysis of isoquinoline-N-Oxide.\textsuperscript{76}

There are three different ways by which the five membered nitrogen heterocycle can be fused with furan nucleus of benzofuran, to produce the following three isomeric benzofuro pyroles. i.e., benzofuro[2,3-c]pyrrole\textsuperscript{77} 11, benzofuro[2,3-b]pyrrole\textsuperscript{78} 12 and benzofuro[3,2-b]pyrrole\textsuperscript{79} 13.
Amongst the various derivatives of the above mentioned heterocyclic systems, benzofuro[2,3-\(c\)]pyrrole have been reported to possess muscle relaxants and tranquilizing property\(^80\). By adopting Fisher indole synthesis, benzofuro[3,2-\(b\)]indole and its derivatives have been synthesized way back in the year 1908\(^{81-82}\).

Schroder \textit{et al.}, reported the synthesis of several derivatives of [3,2-\(b\)]indole 13 and found that many of these synthesized compounds possessed anti-depressant activity\(^83\).

There are several reports in literature in connection with 5-membered ring containing 2-nitrogen atoms, 1-nitrogen and 1-oxygen, 1-nitrogen and 1-sulphur atom and 3-nitrogen atoms.

Thus various derivatives of benzofuropyrazoles, benzofurooxazoles, benzofurothiazoles and benzofurotriazoles have been synthesized and evaluated for various activities. However, keeping in view, the limitations of this thesis only structures of such compounds with relevant references are given below.

\textbf{i. Benzofuro[3,2-\(c\)]pyrrole} \(^{84-85}\) 14
ii. Benzofuro oxazoles\textsuperscript{86-87} 15

![Benzofuro oxazole](image)

iii. Benzofuro thiazoles\textsuperscript{88-89} 16

![Benzofuro thiazole](image)

iv. Benzofuro triazoles\textsuperscript{90-91} 17

![Benzofuro triazole](image)

Benzofuro-[2,3-\textit{d}]triazole

The 6-membered nitrogen heterocycle, pyridine, like pyrrole can also be condensed with furan nucleus of benzofuran in three different ways to give benzofuro[2,3-\textit{b}]pyridine 18, benzofuro[3,2-\textit{c}]pyridine 19 and benzofuro[3-2-\textit{b}]pyridine 20.

![Benzofuro[2,3-\textit{b}]pyridine](image)  
![Benzofuro[3,2-\textit{c}]pyridine](image)  
![Benzofuro[3-2-\textit{b}]pyridine](image)

Derivatives of these heterocycles have been synthesized by utilizing various synthetic routes and some of these compounds have been found to exhibit anti-inflammatory and bacteriostatic\textsuperscript{92-93}, antiviral\textsuperscript{94-96}, analeptic and analgesic\textsuperscript{97} activities. Some of the derivatives of benzofuro[2,3-\textit{b}]pyridine have been utilized in the manufacture of dyes\textsuperscript{98-99}. 
Amongst the various isomers of condensed heterocycles, in which benzofuran is fused with 6-membered ring containing two-nitrogen atoms i.e., benzofuro[3,2-$d$]pyrimidines have been explored to a maximum extent. Many derivatives of these isomers were found to be useful in inhibiting thrombous formation and they also inhibit collagen induced platelet aggregation in plasma from dogs. As a result of such intensive research, several papers describing synthesis, spectral studies and biological activities of these isomer have appeared in literature in the form of research papers and review articles$^{100-107}$.

Ex: Benzofuro[3, 2-$d$]pyrimidine 21

![Benzofuro[3, 2-$d$]pyrimidine 21](image)

Even though, the chemistry of compounds where in benzofuran is condensed with seven-membered heterocycles containing one, two or three nitrogen atoms has not been received much attention of chemists, there are some interesting reports regarding synthesis of benzofuro azepine 22, benzofuro diazepine 23 and benzofuro triazepine 24 due to their significant tranquilizing$^{108}$, sedative and CNS-depressant activities.

Benzofuro azepine

![Benzofuro azepine 22](image)
Benzofuro diazepine

![](image1)

Benzofuro triazepine

![](image2)

Many of such compounds are also found to be associated with vasodilator, hypnoanalytic, anticonvulsant and antiinflammatory activities. Some of these compounds are well known to possess herbicidal and pesticidal properties.

3. Naphthofurans

3.1 Naturally occurring naphthofuran compounds

Benzofuran and naphthofuran nuclei are key structural moieties found in a large number of biologically important natural products, mainly belonging to the sesquiterpene and arylquinone classes. Many of naphthofuran containing compounds such as (dl) laevigatin, (+)-heritol and balsaminone-A possess interesting pharmacological and cytotoxic properties.
Some of the naphthofuran derivatives are reported to occur in the form of naphthofuro quinines, in few medicinal plants. Manasonone D- and Dumnione 28 have been isolated from leaves of *Mansonia lissma* (*Straculiaceae* family) and *Streptocarpus dunniimast* respectively. The compounds were identified as 3,4,5-trimethyl, 2,3-dihydronaphtho[2,1-b]furan-5,6-dione and 2,3,3-trimethynaphtho[1,2-b]furan-4,5-dione on the basis of spectral studies\textsuperscript{119-122}.

As a mixture of d and l-enantiomers, dumnione was also found to be present in plant *Calceolaria integrifolia*\textsuperscript{123}.

After extensive research work on plant *Tabebuia impetiginosa*, Fujimoto *et al* isolated and identified one compound 5-hydroxy-2-(1-hydroxyethyl)naphtho[2,3-b]furan-4-9-dione on the basis of spectral and X-ray crystallographic studies\textsuperscript{124}.

Abdo *et al.*, isolated natural analogues of naphthofurans from the roots of senecio canescenes namely 13-hydroxy cacalohastine and 13-acetoxydehydro-cacalohastine along with some sesquiterpenoids. In their recent communication, Japanese workers reported isolation of 14-methoxy de-hydrocacolohestine from *Trichilo cuneata*\textsuperscript{125}.

Rubicardiofolian 29 is a natural product found in Chinese medicinal plant *Rubiocordifolia* which is known for its cytotoxic activity i.e., found to contain the following compound encompassing naphthofuran nucleus as on of the components\textsuperscript{126}.
Heartwood of *Tabebuia pentaphylla* as found to contain many derivatives of 2-acetylnaphtho[2,3-\(b\)]furan-4, 9-dione\(^{30}\).

Various derivatives of 2-acetylnaphtho[2,3-\(b\)]furan-4-9-dione were reported to be present in the trunk wood of seven different plant species of *Taberlubia*\(^{127-129}\). In the form of its quinone, naphtho[2,1-\(b\)]furan was found to be present as aglycon, in wood parts and roots of various plants belonging to nineteen plant families, which demonstrates the existence of naphthofuran in wide range of plants\(^{132}\).

### 3.2 Synthetic naphthofurans

Naphthofurans either fused or coupled with nitrogen heterocycle do not occur in nature. Even, such synthetic naphthofurans are not reported so far except, some reports from our laboratory\(^{133-143}\).

These synthesized compounds have been found to be associated with wide range of biological and pharmacological activities such as antibacterial, antifungal, anthelmintic, analgesic, diuretic and antiinflammatory.
The first synthesis of naphthofuran was reported by Stoermer\textsuperscript{144}, since then investigation on naphthofurans has not received much attention of organic chemists.

Amongst the several isomers of naphthofurans, only the following four isomers, naphtho[2,1-\textit{b}]furan \textbf{31}, naphtho[1,2-\textit{b}]furan \textbf{32}, naphtho[2,3-\textit{b}]furan \textbf{33} and naphtho[3,2-\textit{b}]furan \textbf{34} and their derivatives are found to exists in nature and hence became a subject of synthetic interest to some chemists.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{31_32_33_34.png}
\caption{Structures of naphthofuran isomers.}
\end{figure}

Hence, it is felt necessary and appropriate to give a brief introduction and literature survey about the investigations carried out on these isomers of naphthofuran.

\subsection{Derivatives of naphtho[2,1-\textit{b}]furan:}

Stoermer was the first scientist to achieve the synthesis of 1-naphthyloxyacetaldehyde\textsuperscript{145}.

The synthesis of 2-acetynaphtho[2,1-\textit{b}]furan was accomplished by the same scientist by the reaction between 2-hydroxy-1-naphthaldehyde in presence of dry benzene and metallic sodium. However, the yield obtained was found to be not satisfactory. After a gap of nearly 54 years Immott and Livingstone reported the synthesis of naphtho[2,1-\textit{b}]
furan-2-carboxylic acid by reacting 2-hydroxy-1-naphthaldehyde with ethyl bromoacetate in the presence of acetic anhydride and sodium acetate. However, they could not isolate the important intermediate ethyl naphtho[2,1-b]furan-2-carboxylate. An interesting report regarding synthesis of the parent heterocycle naphtho[2,1-b]furan 35 by photo cyclo-dehydrogenation of 2-styryl furan appeared in literature.

![Diagram](image)

The various metal complexes using derivatives of naphtho[2,1-b]furan have been shown to exhibit antimicrobial, anthelmintic, analgesic and antiinflammatory activities.

Some of the derivatives of naphtho[2,1-b]furan were found to increase sexual maturation in male rats during neonatal period. When compared to classical estrogens these derivatives of naphthofurans retard the growth of testes and accessory organs and does not effect spermatogenesis and effect on brain is less.

There are reports in literature in connection with nitro derivatives of naphtho[2,1-b]furan 36. L.Cui et al., synthesized 2-nitro-7-methoxynaphtho[2,1-b]furan which was found to be very potent mutagen that causes sarcomas in the fore stomach when injected subcutaneously to albino rats.

It has been demonstrated that 2-nitro-8-methoxynaphtho[2,1-b]furan 37 and 2-nitro-7-bromonaphtho[2,1-b]furan 38 exhibit considerable mutagenic activity. The influence of methoxy and nitro groups in oxidative metabolism has been investigated by Strapelias et al., in detail. Substituted 1-[3',4',5',trimethoxy)phenyl naphtho[2,1-b]furan 39 have been found to exhibit considerable anticancer activity against human cancer cell lines in vitro.
Recently Park & Jeong could accomplish the synthesis of 2-cyano-3-phenyl naphtho[2,1-b]furan 40 by base catalyzed cyclisation of ortho-alkoxy benzoyl arenes\textsuperscript{155}.

The coupling reaction between naphthols, aldehydes and carban monoxide in presence of Pd catalyst yielded various derivatives of naphtho[2,1-b]furan-2-(3H)-one\textsuperscript{156}.

Kirimura \textit{et al.}, who achieved the synthesis of naphthofuran by bio-desulfurisation of benzothiophene, extended the similar method of synthesis of naphtho[2,1-b]furan by bio-desulfurisation in presence of \textit{Rhodococcus}\textsuperscript{73}. 
By reacting 2-naphthol with 3-chloro-3-thio-methyl-2-butamine in presence of stannous chloride using dichloromethane as solvent, 2-3-dimethylnaphtho[2,1-b]furan 42 has been synthesised

3.2.2 Derivatives of naphtho[1,2-b]furan

Ebine was the first scientist to report the synthesis of naphtho[1,2-b]furan derivatives in the year 1953. Bernatek investigated the work carried out by Ebine and applied similar procedure to synthesise various derivatives of naphtho[1,2-b]furan by reacting 1,4-naphthoquinones with appropriate β-diketones in presence of methanolic zinc chloride.
Veluchamy and Rao devoted their research work to study the chemistry of various terpenoids. During these investigations, they reported the synthesis 3,6,9-trimethoxy naphtho[1,2-b]furan\textsuperscript{160} 48 which is closely related to Emmotin-G.

![Chemical structure of 48]

By using the following synthetic strategy, Emmott and Livingstone\textsuperscript{161} synthesised 5-methoxynaphtho[1,2-b]furan and 5-methoxynaphtho[1,2-b]furan-2-carboxylic acid 49. Decarboxylation of 49 yielded 5-methoxynaphtho[1,2-b]furan 50.

![Synthetic pathway from 49 to 50]

One step synthesis of naphtho[1,2-b]furan was reported in the literature by using N-(naphthoxybenzotriazoles) as starting material. This method of synthesis involves insertion reaction\textsuperscript{162}. Mukhanova et al., reported synthesis and antimicrobial evaluation of various derivatives of amino methylnaphtho[1,2-b]furan and found that many of the synthesized
compounds exhibited weak to moderate antibacterial and antifungal activities\textsuperscript{163}. They also devised a new method\textsuperscript{164} for synthesizing 2-methyl-3-benzyl-5-hydroxy naphtho[1,2-\textit{b}]furan by reacting 4-naphthoquinones with enamino ketone.

Toshio \textit{et al.}, isolated two compounds from fermentation broth of Nocardia species TP-A0248. They could achieve purification of these compounds by using chromatographic technique and based upon spectroscopic studies, the compounds were identified as derivatives of naphtho[1,2-\textit{b}]furan-4,5-diones. These compounds were found to exhibit moderate antifungal and cytotoxic activities\textsuperscript{165}.

### 3.3.3 Derivatives of naphtho[2,3-\textit{b}]furan

The first report in connection with the synthesis of naphtho[2,3-\textit{b}]furan was due to Immott \textit{et al.}. They could achieve the synthesis of the desired compounds i.e., naphtho[2,3-\textit{b}]furan-2-carboxylic acid and naphtho[2,3-\textit{b}]furan\textsuperscript{166} starting from 3-hydroxy methyl-2-naphthol by the following sequence of reaction.
Starting from methyl 2-hydroxy-naphtho-3-carboxylate 56, the synthesis of ethyl 3-hydroxynaphtho[2,3-b]furan-2-carboxylate 59 was accomplished via the formation of intermediate condensed product\textsuperscript{167}.

An interesting report regarding synthesis of naphtho[2,3-b]furan-4,9-dione, appeared in the literature, which utilizes organo lithium compounds and phthalic anhydride through inverse addition reaction. The intermediate carboxylic acid on reaction with LDA resulted in the formation of expected dione\textsuperscript{168} 60.
Encouraged by these observations the some authors extended this procedure for the synthesis of various 2-substituted naphtho[2,3-b]furan-4, 9-diones\textsuperscript{169-170}.

Kurihara \textit{et al.}, synthesized series of non-steroidal progesterol compounds and studied structure activity relationship. In this connection they made modification at 3, 4, 5, 7 and 9 positions of 6-acetoxy-4a, 5, 6, 7-tetrahydro-3, 4a-5-trimethyl naphtho[2,3-b]furan-2-(4H)-one\textsuperscript{171}.

4. Synthetic benzofuran and naphthofuran compounds coupled with nitrogen and other heterocycles.

The other ways of combining various heterocycles with benzofuran nucleus and naphthofuran nucleus involve direct linkage of both the heterocyclic systems so as to produce biheterocycles and through carbon or nitrogen bridge. These types of mixed heterocycles with benzofuran, as one of the component, are of much interest to explore biological activities. Several research workers have tried to design and synthesize such molecules in search for potent drug. As a result of such investigations, number of papers
have appeared describing synthesis, characterization and biological evaluation of various biheterocycles encomposing benzofuran and five membered heterocycles such as furan, pyrrole, pyrazole, imidazole, pyrazoline, isoxazole, isoxazoline, thiazole, oxadiazole. Most of such work has come up during the last two decades. However, similar type of work on naphthofuran has not been reported in literature, except some reports from our laboratory\textsuperscript{141-143}.

However, the detailed discussion of such work is out of the scope of this thesis. Hence, only the important reports mentioning the structure, biological activity and references are presented in Table-1.1.
<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Structure of compound</th>
<th>Reported activities and uses</th>
<th>Ref. No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="image1.png" alt="Structure of compound 1" /></td>
<td>Possess antibacterial activity. The minimum inhibitory concentration (MIC) of all these compounds is 2.5-100 mg/ml for <em>E. coli</em>, <em>B. subtilis</em>, <em>P. aureginosa</em> and <em>S. aureus</em>. The MIC value of these compounds for <em>C. albicans</em> is 100 mg/ml.</td>
<td>172</td>
</tr>
<tr>
<td>2</td>
<td><img src="image2.png" alt="Structure of compound 2" /></td>
<td>Possess antihypertensive activity in rats.</td>
<td>173</td>
</tr>
<tr>
<td>3</td>
<td><img src="image3.png" alt="Structure of compound 3" /></td>
<td>Useful in the treatment of fear in emotions of psychogenic origin.</td>
<td>174</td>
</tr>
<tr>
<td>4</td>
<td><img src="image4.png" alt="Structure of compound 4" /></td>
<td>Possess insecticidal and miticidal activity</td>
<td>175</td>
</tr>
</tbody>
</table>
In the form of acid salts, they are useful in antidepressant preparations.

Found to be useful as fluorescent whitners for arcylic and polyester fibres.

Inhibitor properties against *Trycophyn mentagrophytes* were studied and some of the compounds were found to have minimum inhibitory concentration of 3 mg/ml.

Reported to exhibit good antibacterial activity.

R = H, Br, R₁= H, OMe, Cl, R₂=H, Me
<table>
<thead>
<tr>
<th>Chapter-1</th>
<th>28</th>
</tr>
</thead>
</table>
| **9**     | ![Chemical Structure 1]  
Ar = C₆H₅, 4-Cl-C₆H₄, 4-NO₂-C₆H₄, 4-OCH₃-C₆H₄, C₄H₃O  
Reported as mono amino oxidase inhibitor. 180 |

Some of these compounds reduce the blood pressure of hypertensive rats by 50 mm Hg 181

| **10**    | ![Chemical Structure 2]  
R=H, Alkyl, Alkoxy carbonyl, CN.  
R₁=H, alkyl; R₂= H, Halo,  
mₙ=1,2; mₙ=3,4.  
Reported to exhibit good antibacterial activity. 182 |

| **11**    | ![Chemical Structure 3]  
R=H, Br  
R₁= H, OMe, Cl, R₂ = H, Me |

Note: The structures and formulas are diagrammed to represent the compounds described in the text.
Possess useful properties like vasodilation and are reported to protect against vasopressin-induced angina and antiarrhythmic. At 5 mg/kg in dogs has 136% increase in cerebral blood flow and at 15 mg/kg in rats has protection against CHCl₃ induced fibrillation.

Possess *in vitro* antimicrobial activity against *S.aureus* and *E.coli* at a concentration of 100 μg.

Reported to exhibit antimicrobial activity against bacteria *S.aureus* and *K.pneumoniae* and fungi *A.niger*.

Reported to exhibit antimicrobial activity against bacteria *S.aureus* and *K.pneumoniae* and fungi *A.niger*.
References:


51. “Indian Pharmacopoeia”, Controller of Publications, Delhi, India, 1996, 1, 495.


