PREFACE

Heterocyclic chemistry in the most challenging and a handsomely rewarding field of study, since it always attracts the attention of scientists working not only in the area of natural products but also in synthetic organic chemistry. Moreover, in tune with the present trend "scientists to the door steps of common man", there is always a challenging and rewarding task in search of more and more new scientific accomplishments. This is reflected by the voluminous data available in the literature on heterocyclic chemistry. Many useful drugs indeed have emerged from such investigations which strengthens the trend. Spectacular advanced has been made in this field to furtherance the knowledge of relationship between chemical structure and biological activity. Thus, the successful application of this class of compounds in various fields ensures a limitless scope for the development of structurally novel compounds with a wide range of physico-chemical and biological properties.

Amongst different heterocyclic systems, the chemistry of five membered heterocycles with more than one heteroatom has gained importance as many of the them exhibit pronounced bioactive nature. One such type of compounds includes pyrazoles and pyrazolines. Hence, any attempt to study their detailed chemistry would add new dimensions to the existing knowledge. Pyrazolones, pyrazoles and related heterocycles posses various types of biological activities. A good deal of importance is given to pyrazolone derivatives. It is due to their wide use in medicinal chemistry and some of them possess antituberculosis, antineoplastic, antidiabetic, antifertility and antityroid activity. In this perspective, a study on "Synthesis, spectral, and bioactive studies on some pyrazolone derivatives", have been taken up and incorporated in the thesis.

The research work embodied in this planned to synthesize some new pyrazolone heterocycles in order to assess their antimicrobial profile. The plan of work consists of synthesis, characterization, antimicrobial activity, and experimental details, which are incorporated in nine chapters. The thesis consists of nine chapters and at the end of each chapter literature citations are given.
The important aspects, experimental results and structural elucidations are briefly described in the part of thesis. Each of the chapters are divided into different sections. The experimental data are presented in the form of tables and a good number of spectra are shown in figures.

CHAPTER – I : Brief review on chemistry of pyrazoles and its derivatives

A five membered cyclic diene containing three carbons and two nitrogens is called a diazole. If two nitrogen atoms are adjacent, it is known as a pyrazole. If one double bond is present, it is a pyrazole. Several types are possible, depending on the substituents to pyrazole ring. Amongst the all types of pyrazole the chemistry of pyrazolone 2 has received much attention in the recent past due to their industrial and pharmacological applications.

\[
\begin{align*}
\text{Pyrazole} & : \quad \text{R} & \quad \text{N} & \quad \text{R'} \\
\text{Pyrazolone} & : \quad \text{R} & \quad \text{N} & \quad \text{O} & \quad \text{R'} & \quad \text{R''}
\end{align*}
\]

In this chapter the general methods of synthesis of pyrazoles and pyrazole derivatives are presented under three different headings.

1. Synthesis of pyrazoles by hydrazine based reactions.
2. Synthesis of tolylazo heterocyclic pyrazoles.

CHAPTER – II : Synthesis of certain novel Mannich bases bearing pyrazole moiety

A review of literature concerning to the synthesis and biological activity of Mannich bases is depicted in the preceding section of this chapter. The need for the present study has been outlines. In this chapter we reported the synthesis and characterization of
I. (4Z)-2-(4-((15Z)-4-(2-phenylhydrazono)-4,5-dihydro-3-methyl-5-oxopyrazol-1-yl) phenylamino)-N'-(2-oxoindolin-3-ylidene) acetohydrazide.

II. (4Z)-2-(4-((15Z)-4-(2-phenylhydrazono)-4,5-dihydro-3-methyl-5-oxopyrazol-1-yl) phenylamino)-N'-(2-oxoindolin-3-ylidene) acetohydrazide.

III. (4Z)-2-(4-((15Z)-4-(2-phenylhydrazono)-4,5-dihydro-3-methyl-5-oxopyrazol-1-yl) phenylamino)-N'-(2-oxo-1-((piperidin-1-yl) methyl) indolin-3-ylidene) acetohydrazide.

The structures of these newly synthesized compounds 45, 47 and 48 were established on the basis of their elemental analysis and spectral (IR, 1HNMR and MS) data.

CHAPTER–III : Synthesis of certain novel 1,3,4-oxadiazoles containing pyrazole moiety

In this chapter, the synthesis of 1,3,4-oxadiazole pyrazol-3-one are presented. In the preceding part of this chapter the general methods of synthesis and biological importance of 1,3,4-oxadiazoles are briefly summarized. The need of the present work has been outlined. In this chapter we described the synthesis and characterization of


II. (4E)-4-(2-substituted aryl hydrazono)-1-{4-[4-acetyl-4,5-dihydro-5-methyl-5-phenyl-1,3,4-oxadiazol-2-yl]aminomethyl]phenyl}-3-methyl-1H-pyrazol-5(4H)-one

The structural assignments to compounds 71 and 72 were based on their elemental analysis and spectral (IR, 1HNMR and MS) data.

CHAPTER–IV : Mannich bases containing [1,3,4]oxadiazole and pyrazole-3-moiety

This chapter deals with synthesis of Mannich bases bearing [1,3,4]-oxadiazole and pyrazol-3-one moiety. In the preceding section of this chapter a brief review of literature concerning the synthesis and biological activity of Mannich bases are incorporated. Chapter IV describes the synthesis and characterization of
I. \((4Z)-4-(2\text{-substituted aryl hydrazono})-1\{-4-[(5\text{-thioxo-4,5-dihydro-1,3,4-oxadiazol-2-yl})methylamino]phenyl\}-3\text{-methyl-1H-pyrazol-5(4H)-one}\ 17.

II. \((4Z)-4\text{-(2-substituted aryl hydrazono)-1-}\{4\text{-(5-thioxo-4-(alkyl/aryl/heterocyclicamino)methyl-4,5-dihydro-1,3,4-oxadiazol-2-yl})methylamino\}phenyl\}-3\text{-methyl-1H-pyrazol-5(4H)-one}\ 18\text{ (Mannich bases).}

The structural assignments to compounds 17 and 18 were based on their elemental analysis and spectral (IR, \(^1\text{HNMR and MS})\ data.

CHAPTER – V : Synthesis of thiozoles containing pyrazolone moiety

In this chapter, the synthesis of thiozoles bearing pyrazolone moiety are presented. A review of literature concerning to the synthesis and biological activity of thiozoles is depicted in the preceding section of this chapter. The need for the present study has been outlined. This chapter consists of synthesis and characterization of

I. \(2\{-4-[4\text{(2-phenylhydrazono)}-4,5\text{-dihydro-3methyl-5-oxopyrazol-1-yl}]\text{phenylamino}\}-\text{aceto thiosemicarbazide}\ 47.

II. \(2\{-4-[4\text{(2-phenylhydrazono)}-4,5\text{-dihydro-3methyl-5-oxopyrazol-1-yl}]\text{phenylamino}\}-N^\prime\{4\text{-substituted thiazol-2-yl}\})\text{aceto hydrazide}\ 48.

The structure of these newly synthesized compounds 47 & 48 were established on the basis of their elemental analysis and spectral (IR, \(^1\text{HNMR and MS})\ data.

CHAPTER–VI : Microwave assisted synthesis of [1,3,4] oxadiazoles containing Pyrazolone moiety

Now a days there is considerable interest in the organic reactions assisted by microwave irradiation. Use of microwave ovens in the organic synthesis can enhance the reaction rates, shorten the reaction time and gives better yields as compared to the conventional heating. In view of the importance of microwave radiation in organic synthesis, we have preformed synthesis of [1,3,4] oxadiazoles under microwave irradiation using phosphorous oxychloride as a oxidizing agent. In this chapter we presented the microwave promoted synthesis and characterization of
The structural assignments to compound 91 were based on their elemental analysis and spectral (IR & ¹HNM R) data.

**CHAPTER-VII : Antimicrobial studies**

All the synthesized compounds were screened for antimicrobial studies against antibacterial and antifungal activity by disc diffusion and MIC by serial dilution method. All the synthesized compounds were subjected to preliminary antibacterial screening by disc diffusion method against *Staphylococcus aureus* NCCS 2079, *Bacillus cereus* NCCS 2106 (gram positive) and *Escherichia coli* NCCS 2065, *Pseudomonas aeruginosa* NCCS 2200 (gram negative).

1,3,4-oxadiazoles containing pyrazol-3-one moiety (10a-j) exhibit moderate anti bacterial activity against the tested organism at the concentration of 250 µg/ml. 1,3,4-oxadiazole system containing chloro (10e, 10h), bromo (10f) and nitro(10j) showed more activity against *Staphylococcus aureus*, *Bacillus acillus careus*, *Escherichia coli*, *Pseudomonas aeruginosa* than other substituted compounds.

Mannich bases containing [1,3,4] oxadiazole and pyrazol-3-one moieties (13a-k) showed good antibacterial activity against the tested organism at the concentration of 250 µg/ml. In this series p-fluoro(13c), p-chloro(13d), p-bromo(13e), p-nitro(13f) and morpholinyl (13i), showed more biological activity than other compounds of the series.

Thiozoles containing pyrazole-3-one moiety (15a-j) showed antibacterial activity against the tested organism at the concentration 100 µg/ml. in the series p-nitro (15e), p-chloro (15f) and p-bromo (15g) compounds showed more antibacterial activity than other compounds of the series.

Mannich bases containing 1,3,4-oxadiazole and pyrazole-3-one moiety (13a-k) show good anti fungal activity against *Aspergillus Niger* NCCS 1196 and *candida alibicans* NCCS 3471, Mannich bases containing 4-F (13c), 4-Cl (13d), 4-Br (13e), 4-
NO\textsubscript{2} (13f) and morpholinyle (13i), compounds showed good antifungal activity against Aspergillus niger and candida albicans at the concentration of 250 \(\mu\)g/ml. The other Mannich bases exhibit moderate activity under similar experimental conditions.

CHAPTER-VIII: Synthesis of certain novel quinoline derivatives containing 1,3,4-oxadiazoles

A review of brief literature concerning 2-methyl tetrahydro quinoline is presented in the preceding pages of this chapter. The need for the present study has been outlined and in this chapter we report a very interesting and a facile synthesis of 1-(6-bromo-1,2,3,4-tetrahydro-2-methylquinolin-4-yl)pyrrolidin-2-ones 17 via 4-nitrophthalic acid catalyzed hetero (4+2) cyclization addition reaction between aryl amines and N-vinyl pyrrolidin-2-one.

The compound 1-(6-bromo-1,2,3,4-tetrahydro-2-methylquinolin-4-yl)pyrrolidin-2-ones 17 is further converted into 1,3,4-oxadiazole and in this chapter we report the synthesis and characterization of

1. cis-ethyl2-[6-bromo-3,4-dihydro-2-methyl-4-(2-oxopyrrolidin-1-yl)quinolin-1(2H)-yl] acetate 9.
2. cis-2-[6-bromo-3,4-dihydro-2-methyl-4-(2-oxopyrrolidin-1-yl)quinolin-1(2H)-yl] acetoxydrazide 10.
3. cis-2-(6-bromo-3,4-dihydro-2-methyl-4-(2-oxopyrrolidin-1-yl)quinolin-1(2H)-yl)-N'-(1-phenylethylidene)acetoxydrazide 11.

The structural assignments to cis-2-(6-bromo-3,4-dihydro-2-methyl-4-(2-oxopyrrolidin-1-yl)quinolin-1(2H)-yl)-N'-(1-phenylethylidene)acetoxydrazide 11 and cis-1-{1-[(4-acetyl-4,5-dihydro-5-methyl-5-phenyl-1,3,4-oxadiazol-yl)methyl]-6-bromo-1,2,3,4-tetrahydro-2-methylquinolin-4-yl}pyrrolidin-2-one 12 were based on their elemental and spectral data (IR, \(^1\)HNMR, MS).
CHAPTER IX: Mannich bases containing 1,3,4-oxadiazoles and tetra hydroquinoline

This chapter deals with synthesis of Mannich bases bearing [1,3,4] oxadiazole and tetra hydroquinoline moiety. Chapter IX describes the synthesis and characterization of

I. Cis-1-{6-bromo-1,2,3,4-tetrahydro-1-[(4,5-dihydro-5-thioxo-1,3,4-oxadiazol-2-yl) methyl]-2-methylquinolin-4-yl} pyrrolidin-2-one 13.

II. Cis-1-{1-[(4-((p-substituted aryl amino) methyl)-4,5-dihydro-5-thioxo-1,3,4-oxadiazol-2-yl) methyl]-6- bromo-1,2,3,4-tetrahydro-2-methylquinolin-4-yl} pyrrolidin-2-one 14 (Mannich bases).

The structural assignment to compounds 13 and 14 was based on elemental analysis and spectral data (IR, 1H NMR, MS).