Synopsis
SYNOPSIS OF THE THESIS TO BE SUBMITTED TO
BHAVNAGAR UNIVERSITY FOR PH. D. DEGREE
IN CHEMISTRY

FACULTY : SCIENCE

TITLE : SYNTHESIS OF MEDICINALLY
        IMPORTANT FUSED OXA, AZA AND
        THIA HETEROCYLCLES

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**Synopsis**

“**Synthesis of Medicinally Important Fused Oxa, Aza and Thia Heterocycles**”

**Introduction:**

In the early nineteenth century, organic chemistry was developed as a part of the human life, and without organic chemistry it is difficult for mankind to survive. Heterocyclic chemistry is one of the branches of Medicinal Chemistry and large numbers of heterocyclic compounds are successfully used as antimicrobial agents. Heterocyclic systems are encountered in many groups of organic compounds possessing great applicability in several industries as well as other aspects of life. Many antibiotics like penicillin, gentamycin, streptomycin, ciprofloxacin, norfloxacin, etc. contain heterocyclic ring systems.

Medicinal Chemistry is a highly interdisciplinary science whose fundamental roots lie in all branches of chemistry and biology. It also concerns with computational chemistry, statistics, molecular biology and pharmacology. It involves the identification, synthesis and development of new chemical entities suitable for therapeutic use. It is also concerned with essentially understanding, explanation of the mechanism and mode of action of the drugs. Heterocyclic Organic Chemistry and the Medicinal Chemistry share a venerable common history. The use of natural and synthetic heterocyclic chemistry is to create molecules that will alter in a useful way to some disease processes in a living system. It also includes the study of existing drugs, their biological properties, and their structure activity relationships, thus we can say heterocyclic organic chemistry is a way, to search a new medicinally active compounds. Therefore in the thesis, we have synthesized and characterized some new medicinally important oxa, aza and thia heterocyclic compounds for their biological evaluation.

The work to be presented in the thesis for the Ph. D. degree has been divided into seven chapters:

Chapter-1 : Introduction of Heterocycles.
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Chapter-3 : Studies of substituted isoxazolo[5,4-d]pyrimidin-4(5H)-one
Chapter-5 : Studies of substituted [1,2,4]triazolo[3,4-a]isoquinoline.
Chapter-6 : Biological evaluation of the synthesized compounds.
Chapter-7 : A comprehensive summary of the work carried out.

Chapter-1:
In this chapter we will discuss the importance of Heterocyclic Chemistry and its significant features in the Medicinal Chemistry.

Chapter-2:
Pyrimidines, being an integral part of DNA and RNA, exhibit diverse pharmacological properties as effective bactericide, fungicide, vermicide and insecticide. Certain pyrimidines and annulated pyrimidine derivatives are also known to display anticancer, antimalarial, antileishmanial and antifilarial activities. Some furans are shown to be useful for the inhibition of thrombin formation. Furans have also been extensively investigated for their pharmacological uses. Some heterocyclic systems constructed on furan, possess anti hypertensive, antiallergic and antidepressant activities. Recently furopyrimidine’s has been discovered as potent dual inhibitor of Tie-2 and VEGFR2 receptor tyrosine kinases. The biodynamic properties of these ring system prompted us to design a system which combines these biolabile components in ring together to give compact structures for screening their antimicrobial activities.

In this chapter we have synthesized various substituted pyrido[3′,2′:4,5]furo[2,3-d]pyrimidine derivatives and its general structure is as follows,
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Where, R= methylamine, ethylamine, piperidine, 3-cyano azetidine, 3-methoxy pyrrolidine, 4-piperidone, morpholine, piperazin-2-one and thiomorpholine

Chapter -3:

Isoxazole is one of important heterocyclic units, which has been widely used as a key building block of pharmaceutical agent. Its derivatives are endowed with many pharmacological properties, such as hypoglycaemic, analgesic, anti-inflammatory, antibacterial, anti-HIV and anticancer activities, as well as useful activities in conditions like schizophrenia, hypertension and alzheimer’s disease. In addition, they also have agrochemical properties including herbicidal and soil fungicidal activities and they have used as pesticides and insecticides. Thus the synthesis of structurally diverse isoxazole – based small molecules are of great significance.

This chapter deals with the new substituted isoxazolo[5,4-d]pyrimidin-4(5H)-one derivatives and its structure is shown below.

![Chemical Structure](image)

Where, \( R_1 = H, \) triflouro methyl, methyl, methoxy, chloro \& flouro

\( R_2 = H, \) methyl \& methoxy

Chapter -4:

Compounds containing a fused pyrimdine ring have attracted attention in the past few years owing to their wide range of biological activity, particularly in cancer and virus research. Among these heterocycle, the thienopyrimidine class is also of interest because some derivatives such as Tiprinast have been show to clinically effective antiallergics. In addition, antianaphilactic, anti-inflammatory analgesic, antipyretic and antineiplastic activities have been described for these compounds.
In this chapter we have synthesized various new 7,9-dimethyl-8-substituted pyrido[3′,2′:4,5]thieno[3,2-d]pyrimidin-4-amine derivatives and its structure is as follows.

Where, R = allyl, ethyl, benzyl, methyl, propyl, butyl, p-methylbenzyl & p-methoxybenzyl

Chapter -5:

8,9-Dimethoxy-s-triazolo-[3,4-a]-isoquinoline and its 3-methyl derivative exhibited anti aggressive activity and specifically inhibited the aggressive response in mouse killing and septal lesioned rats, a doses below those produce evidence of neutrotoxicity. Anti-inflammatory s-triazolo-[3,4-a]-isoquinoline are active against various forms of arthritis, edemas etc. in man and mammals. 3-Chlorodifluromethyl-s-triazolo-[3,4-a]-isoquinoline and 3-trifluoromethyl-5,6-dihydro-s-triazolo-[3,4-a]isoquinoline were useful as antiflammatory agents and also possessed antiseretary activity. Pregnancy termination in dogs was studied with novel non-hormonal compound 2-(3-ethoxyphenyl)-5,6-dihydro-s-triazolo-[5,1-a]-isoquinoline. 2-(4-Chlorophenyl)-5,6-dihydro-s-triazolo-[5,1-a]-isoquinoline could be used to terminate unwanted pregnancies in Beagle bitches without adversely affecting the reproductive cycle or fertility of the animal. s-Triazolo-[3,4-a]-isoquinoline and its 3-substituent derivatives are also useful as coronary dilating agents. They also possess good cardiovascular activity. s-Triazolo-[5,1-a]-isoquinolines and their derivatives are useful as antioxidants and corrosion inhibitors. s-Triazolo-[3,4-a]-isoquinolines act as a development-promoting agents in photography. In view of the interesting properties exhibited by s-triazolo-[3,4-a]-isoquinolines it was thought worthwhile to explore for their synthesis which has general applicability.
In this Chapter various new [1,2,4]triazolo[3,4-a]isoquinoline of the following structure have been synthesized.

\[
\begin{align*}
\text{Where, } & R_1 = \text{methoxy & methyl;} \\
& R_2 = \text{H, methoxy & methyl;} \\
& R_3 = \text{methyl & phenyl;} 9\text{-methoxy-3,6-dimethyl-} [1,2,4] \text{triazolo[3,4-a]isoquinoline.}
\end{align*}
\]

**Chapter-6:**
This chapter deals with the biological evaluation of the synthesized compounds.

**Chapter-7:**
Comprehensive summary of the work carried out.

**Signature of the Candidate**
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**Signature of the Guide**
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**Place:** Bhavnagar