Work Plan and Methodology:

(1) Work Plan:

<table>
<thead>
<tr>
<th>Year</th>
<th>Months</th>
<th>Task</th>
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<tbody>
<tr>
<td>1st Year</td>
<td>1st</td>
<td>To Review Research Article</td>
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<tr>
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<td>2nd</td>
<td>To synthesize chalcones derivatives</td>
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<tr>
<td>2nd Year</td>
<td>1st</td>
<td>To synthesize pyrazoline,pyrimidines derivatives</td>
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<td>2nd</td>
<td>Spectral studies and Biological evaluation</td>
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(2) Methodology:

A. To carry out literature survey about work done on the selected heterocyclic systems.

B. Synthesis of newer heterocyclic system.

The work to be presented in the thesis has been divided into three derivatives:

**STUDIES ON CHALCONES**

The chemistry of chalcone has generated intensive scientific studies throughout the world. The biological and industrial applications of chalcones are also significant. The chalcone containing an active keto-ethylenic linkage are well known intermediates in the synthesis of heterocyclic compounds.

\[
\begin{align*}
\text{R} & = \text{Cl, Br,} \\
\text{R}^1 & = \text{H, 3-Br, 4-OCH}_3, 3-\text{Cl, 4-CH}_3, 2-\text{Cl, 4-Cl, 3,4 di-OCH}_3, 2,4 \text{ di-OCH}_3
\end{align*}
\]

A mixture of 1-(3-bromo-5-methylphenyl)ethanone (0.01 mole) and various benzaldehyde (0.01 mole) in ethanol (30 ml) was added a solution of potassium hydroxide (40
ml, 40%), the reaction mixture was stirred for a 24 hours to get desired product 1-(3-bromo-5-chloro-2-hydroxyphenyl)-3-substitutedphenylprop-2-en-1-one (2a-i). The spectral studies include IR, $^1$H NMR, $^{13}$C NMR and LC Mass spectra.

STUDIES ON PYRAZOLINES

Pyrazoline consist a unique class of nitrogen containing five member heterocycle. Literature survey reveals that various they are endowed with wide range of pharmacological activities. In view of these facts, it was contemplated to synthesize some new pyrazoline derivatives, which have been described in the following sections.

Section: 3.1 Synthesis, spectral studies and biological evaluation of Pyrazolines. [3.1a-i]

In this section, 4-bromo-2-chloro-6-(5-substitutedphenyl-4,5-dihydro-1H-pyrazol-3-yl) phenol of type (3.1a-i) have been undertaken by the reaction of pyrazoline of type (3.1a-i) with glacial acetic acid in ethanol.

Section: 3.2

Synthesis, spectral studies and biological evaluation acetyl pyrazolines. [3.2a-i]

In this section, 1-[3-(3-bromo-5-chloro-2-hydroxyphenyl)-5-substitutedphenyl-4,5-dihydro-1H-pyrazol-1-yl]ethanone of type (3.2a-i) have been undertaken by the reaction of pyrazoline of type (3.2a-i) with glacial acetic acid in ethanol.
Section: 3.3

Synthesis, spectral studies and biological evaluation of Propionyl pyrazolines.[3.3a-i]

In this section, 1-[3-(3-bromo-5-chloro-2-hydroxyphenyl)-5-substitutedphenyl-4,5-dihydro-1H-pyrazol-1-yl]propan-1-one derivatives of type-(3.3a-i) have synthesized by the condensation of 1-(3-bromo-5-chloro-2-hydroxyphenyl)-3-substitutedphenylprop-2-en-1-one (2a-i) with hydrazine hydrate in propionic acid.

Section: 3.4

Synthesis, spectral studies and biological evaluation of Butyryl pyrazolines.[3.4a-i]

In this section, derivatives 1-[3-(3-bromo-5-chloro-2-hydroxyphenyl)-5-phenyl-4,5-dihydro-1H-pyrazol-1-yl]butan-1-one of type-(2.4a-i) have synthesized by condensation of 1-(3-bromo-5-chloro-2-hydroxyphenyl)-3-substitutedphenylprop-2-en-1-one (1a-i) with hydrazine hydrate in butyric acid.

Section: 3.5

Synthesis, spectral studies and biological evaluation of 4,5-dihydro-1H-pyrazole-1-carbothioamides.[3.5a-i]
In this section, derivatives 3-(3-bromo-5-chloro-2-hydroxyphenyl)-5-substitutedphenyl-4,5-dihydro-1\textit{H}-pyrazole-1-carbothioamide (3.5a-i) were synthesized by condensation of 1-(3-bromo-5-chloro-2-hydroxyphenyl)-3-substitutedphenylprop-2-en-1-one (2a-i) with thiosemicarbazide in presence of ethanol.

**STUDIES ON PYRIMIDINE**

The study of nitrogen-containing heterocycles is currently a hot topic in medicinal chemistry. In particular the chemistry of pyrimidene derivatives has been of considerable interest for many years. Pyrimidene are of considerable pharmaceutical and material interest. This chapter is divided into five sections.

**Section-4.1**

**Synthesis, spectral studies and biological evaluation of Pyrimidin-2-ol [4.1a-i]**

![Pyrimidin-2-ol structure](image)

In this section, 4-(3-bromo-5-chloro-2-hydroxyphenyl)-6-substitutedphenyl-1,6-dihydropyrimidin-2-ol (4.1 a-i) have synthesized by condensation of 1-(3-bromo-5-chloro-2-hydroxyphenyl)-3-substitutedphenylprop-2-en-1-one (2 a-i) with the condensation of chalcone with Urea in presence of KOH. The spectral studies include IR, $^1\text{H}$ NMR, $^{13}\text{C}$ NMR and LC Mass spectra.

**Section-4.2**

**Synthesis, spectral studies and biological evaluation of Pyrimidin-2-thione. [4.2a-i]**

![Pyrimidin-2-thione structure](image)
In this section, 4-bromo-2-chloro-6-(6-substitutedphenyl-2-sulfanyl-1,6-dihydropyrimidin-4-yl)phenol derivatives of type-(4.2 a-i) have synthesized by condensation of 1-(3-bromo-5-chloro-2-hydroxyphenyl)-3-substitutedphenylprop-2-en-1-one (2 a-i) with thiourea in presence of KOH. The spectral studies include IR, $^1$H NMR, $^{13}$C NMR and LC Mass spectra.

Section-4.3

Synthesis, spectral studies and biological evaluation of Phenylpyrimidine-2(1H)-thione[4.3a-i]

In this section, 4-(3-bromo-5-chloro-2-hydroxyphenyl)-6-(4-substitutedphenyl)-1-phenylpyrimidine-2(1H)-thione derivatives (4.3 a-i) have synthesized by condensation of 1-(3-bromo-5-chloro-2-hydroxyphenyl)-3-substitutedphenylprop-2-en-1-one (2 a-i) with Phenyl thiourea in presence of KOH. The spectral studies include IR, $^1$H NMR, $^{13}$C NMR and LC Mass spectra.

Section-4.4

Synthesis, spectral studies and biological evaluation of 1-(4-methylphenyl)-phenylpyrimidine-2(1H)-thione[4.4a-i]

In this section, 4-(3-bromo-5-chloro-2-hydroxyphenyl)-1-(4-methylphenyl)-6-substitutedphenylpyrimidine-2(1H)-thionederivatives (4.4 a-i) have synthesized by condensation of 1-(3-bromo-5-chloro-2-hydroxyphenyl)-3-substitutedphenylprop-2-en-1-one (2 a-i) with 4-methylphenyl thiourea in presence of KOH. The spectral studies include IR, $^1$H NMR, $^{13}$C NMR and LC Mass spectra.
Section 4.5

Synthesis, spectral studies and biological evaluation of (4-methoxylphenyl)-phenylpyrimidine-2(1H)-thione [4.5a-i]

In this section, 4-(3-bromo-5-chloro-2-hydroxyphenyl)-1-(4-methoxyphenyl)-6-substitutedphenylpyrimidine-2(1H)-thione derivatives (4.5 a-i) have synthesized by condensation of 1-(3-bromo-5-chloro-2-hydroxyphenyl)-3-substitutedphenylprop-2-en-1-one (2 a-i) with 4-methoxyphenyl thiourea in presence of KOH. The spectral studies include IR, $^1$H NMR, $^{13}$C NMR and LC Mass spectra.

All the synthesized compounds were screened for their in vitro antibacterial activity and evaluated MIC against gram positive bacterial strains Staphylococcus aureus [MTCC 96], Streptococcus pyogenes [MTCC 442] and gram negative bacterial strains Escherichia coli [MTCC 443], Pseudomonas aeruginosa [MTCC 1688] at a concentration of 6.25 $\mu$g/ml. The compounds were also screened for their anti fungal activity and evaluated MIC against Candida albicans [MTCC 227] and Aspergillus niger [MTCC 282] at a concentration of 6.25 $\mu$g/ml. The MIC values of synthesized compounds were compared with standard drugs like Gentamycin and K.Nystatin.

The constitution of the synthesized compounds have been characterized by using elemental analysis, IR spectra, $^1$H NMR spectra and further supported by $^{13}$C NMR and LC MASS spectra. Purity of all the synthesized compounds has been checked by thin layer chromatography.