SUMMARY

Heterocyclic chemistry is the most challenging and a handsomely rewarding field of study. Amongst different heterocyclic systems, the chemistry of indole nucleus has gained importance as many of them exhibit pronounced bioactive nature. Indole derivatives have been a topic of substantial research interest and continue to be one of the most active areas of heterocyclic chemistry.

The research work embodied in this thesis is planned to synthesize some new Indole derivatives in order to assess their antimicrobial profile. The plan of work consists of synthesis, characterization, antimicrobial activity and experimental details, which are incorporated in seven chapters. At the end of each chapter typical IR, 1H-NMR, 13C-NMR are incorporated besides literature citations.

Organic synthesis

In the current investigations, we report here in synthesis of indole derivatives containing other active heterocyclics. The important aspects, experimental results and structural elucidations are briefly described in the part of thesis. 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 Indole and its derivatives

Indole is one of the class of organic heterocyclic compounds consisting of a six membered benzene ring fused to a five membered nitrogen containing pyrrole ring through the 2- and 3-positions of the pyrrole nucleus. Indole is called as benzopyrrole.

In this chapter discuss about brief review on indole and the general methods of synthesis of Indole and its derivatives are presented under three different headings.

1. Brief review on indole
2. General methods to Synthesis of Indole nucleus.
3. Biological significance of Indole derivatives

CHAPTER – II: Synthesis of certain novel Indole - Isatin Mannich bases containing Pyrazole moiety

Mannich bases are widely useful in the field of pharmaceutical products. The previous studies reveals that Mannich bases exhibit good anti-inflammatory, anti-analgesic, antimycobacterial, anticancer, anti-HIV, and also remarkable antimicrobial activities. The literature survey reveals that the Mannich bases posses a wide range of biological activities. The present work concerns to the synthesis, characterization and anti-microbial activities of
Mannich bases containing indole derivatives. In this chapter we reported the synthesis and characterization of

- Synthesis of ethyl-2-(3-acetyl-5-chloro-1H-indol-1-yl)acetate (2)
- Synthesis of 2-5-chloro-3-((1-(2-pyridin-4-yl)hydrazono)ethyl)-1H-indol-1-yl)acetate (4)
- Synthesis of ethyl-2-(5-chloro-3-(4-formyl-1-(pyridine-4-yl)-1H-pyrazol-3-yl)-1H-indol-1-yl)acetate (5)
- Synthesis of ethyl-2-(5-chloro-3-(4-substituted phenyl imino)methyl)-1(pyridin-4-yl)-1H-pyrazol-3-yl)-1H-indol-1-yl)acetate (6a-e)
- Synthesis of 2-(5-chloro-3-(4-substituted phenylimino) methyl)-1-(pyridin-4-yl)-1H-pyrazol-3-yl)-1H-indol-1-yl)acetohydrazide (7a-e)
- Synthesis of 2-(5-chloro-3-(4-substituted phenylimino) methyl)-1-(pyridin-4-yl)-1H-pyrazol-3-yl)1H-indol-1-yl)acetohydrazide (8a-e)
- Synthesis of 2-(5-chloro-3-(4-substituted phenylimino) methyl)-1-(pyridin-4-yl)-1H-pyrazol-3-yl)-1H-indol-1-yl)-N\(^1\)-(2-oxoindolin-3-ylidene)acetohydrazide (9a-o)

The structures of these newly synthesized compounds were established on the basis of their elemental analysis and spectral (IR, NMR and Mass) data. The synthetic route is outlined in **Scheme - I**
CHAPTER – III : Synthesis of Indole-1,3,4-oxadiazole azetidine-2-one/ tetrazole derivatives containing Pyrazole moiety

The heterocyclic compounds 1,3,4-oxadiazole azetidine-2-one/tetrazoles are possessing a broad spectrum of biological activities. Thus in this chapter we describe the synthesis and characterization of indol derivatives bearing 1,3,4-oxadiazole azetidine-2-one/tetrazoles. This chapter was divided into two sections.

Present Work : In this chapter we report the synthesis and characterisation of

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<th>9b/9g/9l</th>
<th>9c/9h/9m</th>
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Scheme-I:-

- Ethyl 2-(5-chloro-3-(4-(3-chloro-4-oxo-1(4-substitutedphenyl) azetidin-2-yl)-1-(pyridin-4-yl)-1H-pyrazol-3-yl)-1H-indol-1-yl)acetate (2)
- 2-(5-chloro-3-(4-(3-chloro-4-oxo-1-(4-substituted phenyl) azetidin-2-yl)-1-(pyridin-4-yl)-1H-pyrazol-3-yl)-1H-indol-1-yl)acetohydrazide (3)
- 2-(5-chloro-3-(4-(3-chloro-4-oxo-1-(4-substituted phenyl) azetidin-2-yl)-1-(pyridin-4-yl)-1H-pyrazol-3-yl)-1H-indol-1-yl)-N’-(1-(p-substitutedphenyl)ethylidene)acetohydrazide (4a-g)
- 4-(3-(1-((4-acetyl-5-methyl-5-(p-substituted phenyl)-4,5-dihydro-1,3,4-oxadiazol-2-yl)methyl)-5-chloro-1H-indol-3-yl)-1-(pyridin-4-yl)-1H-pyrazol-4-yl)-3-chloro-1-(4-substituted phenyl)azetidin-2-one (5a-g)

Scheme-II:-

- Ethyl-2-(5-chloro-3-(1-(pyridine-4yl)-4-(1-(4-substitutedphenyl)-1H-tetrazol-5-yl)-1H-Indol-1-yl)acetate (2)
- 2-(5-chloro-3-(1-(pyridine-4-yl)-4-(1-(4-substituted phenyl)-1H-tetrazol-3-yl)-1H-Pyrazol-3-yl)-1H-indol-1-yl) acetohydrazide (3)
- 2-(5-chloro-3-(1-(pyridine-4-yl)-4-(1-(4-substituted phenyl)-1H-tetrazol-3-yl)-1H-Indol-1-yl)-N’-(1-(4-substituted phenyl)ethylidene)acetohydrazide (4a-g)
1-(5-((5-chloro-3-(1-(pyridine-4-yl)-4-(1-(4-substituted phenyl)-1H-tetrazol-5-yl)-1H-pyrazol-3-yl)-1H-indol-1-yl)methyl)-2-(4-substituted phenyl)-2-methyl-1,3,4-oxadiazol-3(2H)-yl)ethanone (5a-g)

The structures of these newly synthesized compounds were established on the basis of their elemental analysis and spectral (IR, NMR and Mass) data. The synthetic approach to these compounds is profiled in **Scheme I and Scheme II**.

**Scheme I**

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<th>5b</th>
<th>5c</th>
<th>5d</th>
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**Scheme II**

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<th>5f</th>
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CHAPTER-IV : Synthesis of Indole-Mannich bases bearing azitidinone-2-one / thiazolidin-4-one derivatives

A review of literature concerning to the synthesis and biological activity of azitidinone and thiazolidinone is depicted in the preceding section of this chapter.

Present Work: In this chapter we describe the synthesis and characterization of

- Synthesis of ethyl 2-(5-chloro-1H-indol-3-yl)acetate: - (2)
- Synthesis of 2-(5-chloro-1H-indol-3-yl)acetohydrazide : - (3)
- Synthesis of 2-(5-chloro-1-(4-Substituted piperidin-1-ylmethyl)-1H-indol-3-yl) acetohydrazide: - (4a-b)
- Synthesis of 2-(5-chloro-1-(4-Substituted piperidin-1-ylmethyl)-1H-indol-3-yl)-N'-(4-Substituted benzylidene)acetohydrazide: - (5a-j)
- Synthesis of 2-(5-chloro-1-(4-Substituted piperidin-1-ylmethyl)-1H-indol-3-yl)-N-(3-chloro-2-oxo-4-(4-Substituted phenylazetidin-1-yl)acetamide : (6a-j)
- Synthesis of 2-(5-chloro-1-(4-Substituted piperidin-1-ylmethyl)-1H-indol-3-yl)-N-(4-oxo-2-Substituted phenylthiazolidin-3-yl)acetamide : - (7a-j)

The structures of these newly synthesized compounds were established on the basis of their elemental analysis and spectral (IR, NMR and Mass) data. The synthetic approach to these compounds is profiled in Scheme I

![Scheme I](image-url)
CHAPTER-V : Synthesis of Indole-Mannich bases bearing 1,3,4-oxadiazole-thione- sulphones of pyrrole derivatives

A review of literature concerning to the synthesis and biological activity of thiones is depicted in the preceding section of this chapter. The need for the present study has been outlined at the end of the chapter.

Present Work : In this chapter we describe the synthesis and characterization of

- Synthesis of 2-(5-chloro-1-(4-substituted piperidin-1-ylmethyl)-1H-indol-3-yl) acetohydrazide (2a-d)
- Synthesis of 5-((5-chloro-1-(4-substituted piperidin-1-ylmethyl)-1H-indol-3-yl)methyl)-1,3,4-oxadiazole-2(3H)-thione (3a-d)
- Synthesis of 2-(((1H-pyrrol-2-yl)methylthio)-5-((5-chloro-1-(4-substituted piperidin-1-ylmethyl)-1H-indol-3-yl)methyl)-1,3,4-oxadiazole(4a-d)
- Synthesis of 5-((5-chloro-1-(4-substituted piperidin-1-ylmethyl)-1H-indol-3-yl) methyl)-2-((furan-2-ylmethyl)thio)-2,3-dihydro-1,3,4-oxadiazole(5a-d)
- Synthesis of 5-((5-chloro-1-(4-substituted piperidin-1-ylmethyl)-1H-indol-3-yl) methyl)-2-((thiophen-2-ylmethyl)thio)-2,3-dihydro-1,3,4-oxadiazole(6a-d)
- Synthesis of 2-(((1H-pyrrol-2-yl)methyl)sulfonyl)-5-((5-chloro-1-(4-substituted piperidin-1-ylmethyl)-1H-indol-3-yl)methyl)-2,3-dihydro-1,3,4-oxadiazole (7a-d)
- Synthesis of 5-((5-chloro-1-(4-substituted piperidin-1-ylmethyl)-1H-indol-3-yl) methyl)-2-((furan-2-ylmethyl)sulfonyl)-2,3-dihydro-1,3,4-oxadiazole (8a-d)
- Synthesis of 5-((5-chloro-1-(4-substituted piperidin-1-ylmethyl)-1H-indol-3-yl) methyl)-2-((thiophen-2-ylmethyl)sulfonyl)-2,3-dihydro-1,3,4-oxadiazole (9a-d)

The structures of these newly synthesized compounds were established on the basis of their elemental analysis and spectral (IR, NMR and Mass) data. The synthetic approach to these compounds is profiled in Scheme I
CHAPTER-VI: Synthesis of Indole-pyrazolone-pyrazole bicyclic derivatives

A review of literature concerning to the synthesis and biological activity of pyrazoles is depicted in the preceding section of this chapter. The need for the present study has been outlined at the end of the chapter.

Present Work: In this chapter we describe the synthesis and characterization of

- Synthesis of 5-nitro-2-phenyl-1H-indole-3-carbaldehyde (2a-b)
- (Z)-3-methyl-4-((5-nitro-2-(4-substitutedphenyl)-1H-indol-3-yl)methylene)-1H-pyrazol-5(4H)-one (3a-b)
- 3-(4-methyl-(substitutedpyrazolo[3,4-c]pyrazol-3-yl)-5-nitro-2-phenyl-1Hindole(4a-d)
- 2-(4-chlorophenyl)-3-(4-methyl-(substitutedpyrazolo[3,4-c]pyrazol-3-yl)-5-nitro-1H-indole (5a-d)

The structures of these newly synthesized compounds were established on the basis of their elemental analysis and spectral (IR, NMR and Mass) data. The synthetic approach to these compounds is profiled in Scheme - I,II
CHAPTER– VII : Antimicrobial Studies

All the synthesized compounds were screened for antimicrobial studies against antibacterial and antifungal activity by disc diffusion method and MIC (Minimum Inhibition Concentration) by serial dilution method. For the prepared compounds using amoxicillin and cefaclor as references were subjected to preliminary antibacterial screening by disc diffusion method against *Staphylococcus aureus* NCCS 2079, *Bacillus cereus* NCCS2106 (gram positive) and *Escherichia coli* NCCS2065, *Pseudomonas aeruginosa* NCCS2200 (gram negative).

Ketoconazole as reference was subjected to preliminary antifungal screening by disc diffusion method against *Aspergillus niger* NCCS 1196 and *Candida albicans* NCCS 3471.

The detailed antibacterial and antifungal activities of all synthesized compounds were presented in the form of tables and figures separately.

**Conclusion:**

In the current investigations, we report herein synthesis of new indole derivatives containing other active heterocyclics. The important aspects, experimental results and structural elucidations are briefly described in this thesis. The analytical data are presented in the form of tables and a good number of spectra are shown in figures. Antimicrobial studies were carried out for newly synthesized compounds and their comparative results were presented.