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I
SUMMARY

The work reported in the thesis with the title, “STUDIES ON NOVEL HETEROCYCLIC COMPOUNDS AND THEIR MICROBICIDAL EFFICACY” has been described under the following different chapters.

CHAPTER-I - INTRODUCTION

Chalcone

Chalcones either natural or synthetic are known to exhibit various biological activities. They have been reported to possess antifungal, antibacterial, antimalarial, anti-inflammatory and anticancer qualities. Chalcones have also served as starting materials for the synthesis of more complex medicinal compounds and as substrates for new enantioselective synthetic methods. The presence of a reactive $\alpha,\beta$-unsaturated keto function in chalcones is found to be responsible for their antimicrobial activity, which may be altered depending on the type and position of substituent on the aromatic rings.

Pyrimidine

Pyrimidine derivatives and its related compounds are known to be associated with biodynamic properties. Pyrimidine derivatives are of interest because of their pharmacological properties including anti-HIV, anti-cancer, analgesic, anti-inflammatory and antileishmanial effects. Several synthetic strategies have been reported for the preparation of pyrimidine derivatives.

In medicinal chemistry pyrimidine derivatives have been very well known for their therapeutic applications. The presence of a pyrimidine base in thymine, cytosine and uracil, which are the essential binding blocks of nucleic acids, DNA and RNA is one possible reason for their activity. The literature indicated that compounds having pyrimidine nucleus possess broad range of
biological activities. Like 5-fluorouracil as anticancer; idoxuridine and trifluoridine as antiviral; zidovudine and stavudine as antiHIV, trimethoprim, sulphamethiazine and sulphadiazine as antibacterial; sulphadoxin as antimalarial and antibacterial; minoxidil and prazosin as antihypertensive; barbiturates e.g. Phenobarbitone as sedative, hypnotics and anticonvulsant; propylthiouracil as antihyroid; thionzylamine as H₁-antihistamine; and toxoflavin and fervennuline as antibiotics.²¹

**Quinoline**

Quinolines and their derivatives are very important in medicinal chemistry because of their wide occurrence in natural products²² and drugs.²³ Quinoline alkaloids such as quinine, chloroquin, mefloquine and amodiaquine are used as efficient drugs for the treatment of malaria.²⁴ The quinoline skeleton is often used for the design of many synthetic compounds with diverse pharmaceutical properties. Some 4-substituted quinoline derivatives showed enhanced activity against gram negative bacteria.²⁵-²⁶

In our efforts to discover new chemical pharmacophores which may be responsible for the antibacterial as well as antifungal activity, we have described our studies on the reaction of aromatic aldehyde with aromatic acetophenone to form chalcone which were further reacted with guanidine nitrate to give 4,6-diaryl substituted-2-pyrimidinamine. These compounds were further coupled with 4-chloroquinoline derivative to get corresponding compound pyrimidine - quinoline clubbed molecule.

Considering the versatile chemistry of cyanuric chloride²⁷-²⁹ and its reactions with various nucleophiles such as amines, amino-sulfonamides, alcohols, phenols, etc., the attempts were also made to couple 4-(3'-bromophenyl)-6-(4-methoxyphenyl)-pyrimidin-2-amine with cold brand reactive dyes.

Realizing the medicinal importance of 2-amino-pyrimidine, quinoline and triazine derivatives it was considered worthwhile to incorporate these moieties. It was therefore thought interesting to synthesize the title
compounds with an object of ascertaining whether they could augment the microbicidal efficacy.

The structures of the various synthesized compounds were assigned on the basis of elemental analysis, IR and $^1$H NMR spectral data. These compounds were also screened for antibacterial and antifungal activity.

CHAPTER – II - EXPERIMENTAL

The work reported in this chapter is presented into five sections.

SECTION-I

It deals with synthesis of chalcone. The compounds having following general formula were synthesized.

\[
\text{1-(substituted phenyl)-3-(substituted phenyl)-2-propen-1-one}
\]

where,

- $R = 2,4-(Cl)_{2}, 5-F, 4-Cl, 4-OCH_3, 4-CH_3$
- $R' = 4'-F, 4'-Cl, 3'-NO_2, 3'-Br$

The compounds of this section have been synthesized by condensing various substituted aromatic acetophenone with substituted aromatic aldehyde.

SECTION – II

It deals with synthesis of 4-(substituted phenyl)-6-(substituted phenyl)-2-pyrimidinamine. The compounds having following general formula were synthesized.
The compounds of this section have been synthesized by cyclization of 1-(substituted phenyl)-3-(substituted phenyl)-2-propen-1-one with guanidine nitrate.

**SECTION – III**

It deals with synthesis of 4-chloroquinoline derivatives. The compounds having following general formula were synthesized.

![4-chloro-6-substituted-2-methylquinoline](image)

**SECTION – IV**

This section is further divided into four parts. It deals with the synthesis of N4-[4,6-diaryl substituted phenyl-2-pyrimidinyl]-substituted-4-quinolinamine having the following general formula.
The compounds of this section have been synthesized by condensing 4-(substituted phenyl)-6-(substituted phenyl)-2-pyrimidinamine with 4-chloroquinoline derivative.

Part-A

N4-[4,6-diaryl substituted phenyl-2-pyrimidylnyl]-7-chloro-4-quinolinamine

The compounds of this part-A have been synthesized by condensing 4-(substituted phenyl)-6-(substituted phenyl)-2-pyrimidinamine with 4,7-dichloroquinoline.

Part-B

N4-[4,6-diaryl substituted phenyl-2-pyrimidylnyl]-2,6-dimethyl-4-quinolinamine

The compounds of this part-B have been synthesized by condensing 4-(substituted phenyl)-6-(substituted phenyl)-2-pyrimidinamine with 4-chloro-2,6-dimethylquinoline.
Part-C

N4-[4,6-diaryl substituted phenyl-2-pyrimidinyl]-6-chloro-2-methyl-4-quinolinamine

The compounds of this part-C have been synthesized by condensing 4-(substituted phenyl)-6-(substituted phenyl)-2-pyrimidinamine with 4,6-dichloro-2-methylquinoline.

Part-D

N4-[4,6-diaryl substituted phenyl-2-pyrimidinyl]-6-methoxy-2-methyl-4-quinolinamine

The compounds of this part-D have been synthesized by condensing 4-(substituted phenyl)-6-(substituted phenyl)-2-pyrimidinamine with 4-chloro-6-methoxy-2-methylquinoline.

SECTION – V

The compounds having the following general formula were synthesized.

![Chemical Structure]

The compounds of this section have been synthesized by condensing 4-(3-bromophenyl)-6-(4-methoxyphenyl)-pyrimidin-2-amine with cold brand reactive dye.
CHAPTER – III- SPECTRAL STUDIES

Infrared spectroscopy of some selected synthesized compounds has been carried out using KBr pellets for structural elucidation, particularly function groups present in the compounds.

Nuclear magnetic resonance spectroscopy of some selected synthesized compounds has been carried out. The $^1$H NMR spectra in DMSO-$d_6$ and CDCl$_3$ were recorded on varian Gemini 400 MHz spectrometer and chemical shifts were reported as parts per million (δ ppm) downfield using TMS as an internal standard.

CHAPTER – IV- ANTIMICROBIAL ACTIVITY

Antibacterial activity

Antibacterial activities of all the newly synthesized compounds were studied against Gram-positive bacteria [Staphylococcus Aureus (MTCC96), Streptococcus Pyogenes (MTCC442)] and Gram-negative bacteria [Escherichia coli (MTCC443), Pseudomonas aeruginosa (MTCC424)] at a concentration of 100 μg/ml by agar cup plate method. The test compounds were dissolved in DMF at a concentration of 100 μg/ml using Chloramphenicol and Ciprofloxacin as standards for comparison control experiment was carried out. The area of inhibition zone was measured in mm.

Antifungal activity

All the newly synthesized compounds were also screened for their antifungal activity against Candida albicans (MTCC227), Aspergillus Niger (MTCC282) using the agar cup plate diffusion method by dissolving in DMF at a concentration of 100 μg/ml. The zone of inhibition was measured after 7 days at 20 °C and it was compared with Greseofulvin and Nystatin as standard drugs.

VIII
CHAPTER – V- RESULTS AND DISCUSSION

The results obtained in chapter-IV have been discussed. It has been found that some compounds show significant antibacterial activity and antifungal activity, where as the rest of the compounds show varying activity.
REFERENCES


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Signature of Supervising Teacher                                Signature of Research Student
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**(Dr. A. G. Mehta) (Avnish A. Patel)**