CHAPTER-V

CONCLUSION
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The present work is focused on the synthesis of various heterocyclic compounds as possible antibacterial agents. The antibacterial screening of the synthesized compounds revealed following observations.

Series : 1, 2 & 3

The study of all the three 4,6-disubstituted pyrimidine based series -1 : N-{[4-(2,4-
 dichloro-5-fluorophenyl)-6-(2-chlorophenyl)]-pyrimidin-2-yl]2-(substituted)-acetamide
(DHA-1 to 10), series-2: 4-[(4-(2,4-Dichloro-5-fluorophenyl)-6-(4-methoxyphenyl)-
pyrimidin-2-yl)-1-(arylcarbamoyl)]-semicarbazide (DHB-1 to 9) & series-3 : 4-[(4-(2,4-
Dichloro-5-fluorophenyl)-6-(4-methoxyphenyl)-pyrimidin-2-yl)-1-(arylcarbamothioyl)]-
semicarbazide (DHC-1 to 9) indicates that the compounds have found notable effective
response against Gram-positive strains under the experiment.

The general observations from the structures of the serieses-1, 2 & 3 exhibits
common part i.e. N-substituted acetamides, aryl carbamoyl and aryl carbamothioyl
semicarbazide linked with 4,6-disubstituted pyrimidine template strongly influenced
antibacterial activity.

The following SAR can be noted from the data of table-1,2 & 3.

In case of series-1, piperazine derivative with electron donating group rather than
the electron withdrawing group especially at 1 or 2 position generally increase the
biological activity which may lead to the formation of van der waal attraction between the
methyl group of molecule with active site.

In series-2, presence of electron withdrawing group on the aromatic ring in general
increase the antimicrobial activities rather than compounds having electron donating
group.

Based on these, it will be necessary to optimize the lead compound by inclusion of
chloro group at C-3 & C-4 position at phenyl nucleus of aryl carbamoyl moiety to the basic
pharmacophore studied.
In series-3, presence of electron withdrawing group as well as electron donating group on the aromatic ring at C-3 & C-4 positions in general increases the antimicrobial activities of the tested compounds.

Based on these it will be necessary to optimize that the position of substitutions rather than the electronic nature of the substitutions dictated the activity profile, and better activities were found with substitutions at C-3 & C-4 phenyl nucleus of aryl thiocarbamoyl moiety. In analogous to series-2, alteration of the oxygen to sulphur atom may be beneficial for antibacterial activity.

In all these series -1, 2, & 3 it was clearly observed that not a single compound was found as active as standard drug though the results are promising.

**Series : 4, 5, 6 & 7**

Four series of novel 2,4,6-trisubstituted s-triazines were synthesized and evaluated for their antibacterial activity. Attempts were made to increase antibacterial activity by introducing substituents to an aryl ring of aryl thioureido group series-4 : 2-(N-methylamino)-4-(N,N-dimethylamino)-6-(arylthioureido)-s-triazine (DHD-1 to 10), series-5 : 2-(N-methylamino)-4-(N,N-dimethylamino)-6-(arylsemicarbazido)-s-triazine (DHE-1 to 9), series-6 : 2-(N-methylamino)-4-(N,N-dimethylamino)-6-(arylthiosemicarbazido)-s-triazine (DHF-1 to 9) & series-7 : 2-(N-methylamino)-4-(N,N-dimethylamino)-6-{N-(arylidine)-hydrazinyl}-s-triazine (DHG-1 to 10) lead to different result depending on the nature, position and number of the atoms or group introduced.

In particular, high activity level was observed for compounds possessing chloro group along with 3- methoxy at the terminus position of aryl thioureido part (series-4), inclusion of phenyl ethyl group to the carbamoyl terminus (series-5) may be due to allosteric site of enzyme which causes distortion of the three dimensional structure of enzyme and inhibits its catalytic function.

Alteration of the oxygen atom to sulphur atom, no more deviation of activity is observed (series-6), electron donating groups like 4-methoxy and 3,4-dimethoxy proved
beneficial for antibacterial activity against Gram-positive strains while electron withdrawing is better for only *E. coli* (Gram-negative strain) (series-7).

The general observation is that the Gram-negative strains were not susceptible to the inhibitory effect of the compounds as compared to Gram-positive strains.

It was also observed that though halo or methyl substituent found active in the range of 12.5 to 100 µg/ml but failed to show activity as good as standard drug. It is worthwhile to mention that halo substituent is much more favorable including electron donating group to obtain comparable activity against Gram-positive and Gram-negative strains.

It can be concluded that the above identified s-triazine could be new lead for antibacterial chemotherapy. These molecules may be useful for further optimization in antibacterial chemotherapy.

**Series : 8, 9 & 10**

The study of all the three 6-Nitroquinazoline based series-8 : 1-{2-(6-Nitroquinazolin-4-yl-thio)-acetyl}-4-(aryl)-semicarbazide (DHH-1 to 9), series-9 : 1-{2-(6-Nitroquinazolin-4-yl-thio)-acetyl}-4-(aryl)-thiosemicarbazide (DHI-1 to 9) & series-10 : N-(arylidine)-2-(6-nitroquinazolin-4-yl-thio)-acetohydrazide (DHJ-1 to 10) led to different results.

The impact of various aryl isocyanates, aryl isothiocyanats and arylaldehyde to the basic scaffold was good and substantial. However, alteration of the oxygen (series-8) atom to sulphur atom (series-9) not much change was observed in antibacterial activity. Overall the compounds of this class (series-10) exhibited better activity profile against Gram-positive and Gram-negative strains.

It is also observed that the halo and methyl along with methoxy substituted compounds, sometimes showed reasonable activity. The higher activity of methyl substituted compounds may be due to their better lipophilicity and hyperconjugation effect towards active site. However, the activity of none of the them matched with that of standard drugs.
From the results obtained, it is observed that the led compounds could be optimized by incorporating other halo groups along with methyl and methoxy substituent to phenyl ring may increase the antibacterial activity.