**ABSTRACT**

Heterocycles form by far the largest of the classical divisions of organic chemistry and are of immense importance biologically, industrially and indeed to the functioning of any developed human society. Till today, drug design by molecular manipulation is a productive source of new drugs. Molecular manipulation involves the efforts to combine separate groups having similar activity in one compound by eliminating or substituting new moiety to a parent lead compound, thus making gradual changes in physicochemical properties and biological activities of the compound.

Two or more active moieties can be combined to produce a new chemical entity by molecular manipulation. This results in better removal of side effects and prevents the development of resistance and also increases the pharmacological activity of the new compounds. Compounds so obtained were screened for different biological activities.

After a thorough and meticulous literature survey on various heterocyclic compounds, we planned to select the following list of moieties. They are Quinoxaline, indoloquinoxaline, benzimidazole, benzothiazole and pyrazole.

Till today no work is reported on the combination of the selected moieties so we planned to combine them to enhance their activities and
synthesize new compounds with good yields and beneficial pharmacological effects.

The proposed strategies of the work are given below.

The thesis entitled, “SYNTHESIS AND PHARMACOLOGICAL EVALUATION OF NEW QUINOXALINE COMPOUNDS” has been divided into 7 chapters.

CHAPTER-1: Introduction and Literature background

This chapter deals with brief introduction to the heterocyclic moieties (Quinoxaline, indoloquinoxaline, benzimidazole, benzothiazole and pyrazole) that are selected for the synthesis of novel compounds, their preparation methods, physical properties, chemical characters, importance of heterocyclic ring systems; survey of literature on pharmacologically active Quinoxalines, indoloquinoxalines, benzimidazoles, benzothiazoles and pyrazoles.

This chapter also reviews the scope and importance of the present research and reports the importance of the molecular manipulation. The pharmacological importance of the selected heterocyclic moieties in the present work is enlightened in brief.

CHAPTER-2: Synthesis of new series of Pyrazolo Indolo quinoxaline compounds

This chapter deals with the synthesis of 15 new compounds i.e., (4,5-dihydro-5-(4-substituted phenyl) -3- ((2-((2,3-diphenyl quinoxalin-6-yl) methyl)-6H-indolo[2,3-b]quinoxalin-6-yl ) methyl ) pyrazol-1- yl)
(phenyl) methanone 2.12(a-e), (5-(4-substituted phenyl)-4,5-dihydro-3-((2-((2,3-diphenylquinoxalin-6-yl)methyl)-6H-indolo[2,3-b] quinoxalin-6-yl) methyl) pyrazol-1-yl) (4-hydroxyphenyl) methanone 2.13(a-e), (4-chlorophenyl)(4,5-dihydro- 5-(4-substituted phenyl) -3-((2-((2,3-diphenylquinoxalin-6-yl)methyl)-6H-indolo[2,3-b]quinoxalin-6-yl) methyl) pyrazol-1-yl)methanone 2.14 (a-e).  In this chapter the prepared 2,3 diphenyl quinoxaline (2.7) and indoloquinoxaline (2.8) compounds were fused with methylene bridge. The formed product, 2-((2,3-diphenylquinoxalin-6-yl) methyl) -6H- indolo [2,3-b] quinoxaline, (2.9) was acetylated to give 1-(2-((2,3- diphenyl quinoxalin-6-yl) methyl) -6H- indolo[2,3-b] quinoxaline -6-yl)propan-2-one, (2.10) and then the chalcones, (E) – 4 - ( 4 – substituted phenyl) -1- (2- (2,3 -diphenyl quinoxalin -6- yl) methyl) -6H- indolo [2,3-b] quinoxalin-6-yl) but-3-en-2 – one, 2.11(a-e) were prepared using 5 different aldehydes. The formed chalcones were condensed with different aromatic acid hydrazides to give 15 new pyrazolo indoloquinoxaline compounds i.e., 2.12 (a-e), 2.13(a-e), 2.14(a-e). They were new and were fully characterized based on their I.R, N.M.R and Mass spectral data.

CHAPTER-3: Synthesis of new series of Benzimidazolo pyrazolo quinoxaline compounds.

This chapter deals with the synthesis of 15 new compounds i.e., (4,5-dihydro-5- (4-substituted phenyl) -3-((5-((2,3-diphenylquinoxalin-6-yl) methyl)-1H - benzo[d]imidazol-1-yl)methyl) pyrazol -1-yl)(phenyl)
methanone 3.12 (a-e), (4,5- dihydro-5-(4-substituted phenyl)-3-((5-((2,3- diphenyl quinoxalin-6 -yl )methyl)-1H-benzo[d] imidazol -1-yl) methyl) pyrazol-1-yl) (4-hydroxy phenyl) methanone, 3.13(a-e), (4-chlorophenyl) (4,5-dihydro-5- (4-substituted phenyl)-3- ((5-((2,3-diphenyl quinoxalin -6- yl) methyl)-1H-benzo[d] imidazol-1-yl) methyl) pyrazol-1-yl) methanone 3.14 (a-e). The benzimidazole (3.7) and 2, 3 diphenyl quinoxaline (3.8) were fused with methylene bridge. The formed product, 6- ((1H-benzo [d] imidazol -5-yl) methyl) -2,3-diphenylquinoxaline (3.9) was acetylated to give 1-(5-((2,3 -diphenyl quinoxalin-6-yl) methyl) -1H-benzo[d] imidazol -1-yl)propan-2-one (3.10) and then the chalcones, (E) -4- (4- substituted phenyl) -1- (5- (( 2, 3-diphenyl quinoxalin-6-yl) methyl) -1H- benzo[d]imidazol-1-yl) but-3-en-2-one 3.11(a-e) were prepared using 5 different aldehydes. The formed chalcones were condensed with 3 different aromatic acid hydrazides to give 15 new benzimidazole pyrazolo quinoxaline compounds i.e., 3.12 (a-e), 3.13(a-e), 3.14(a-e). They were purified and fully characterized based on their I.R, N.M.R and Mass spectral data.

CHAPTER-4: Synthesis of new series of Benzothiazolo Pyrazolo quinoxaline compounds.

This chapter deals with the synthesis of 15 new compounds that were not reported earlier i.e., (3-((6-((2,3-diphenylquinoxalin-6-yl)methyl) benzo [d] thiazol-2-ylamino) methyl) -4,5-dihydro-5- (4-substituted phenyl) pyrazol-1-yl) (phenyl) methanone 4.12(a-e), (3- ((6- (( 2,3-
diphenyl quinoxalin-6-yl) methyl) benzo[d] thiazol-2-ylamino)methyl)-4,5-dihydro-5-(4-substituted phenyl) pyrazol-1-yl) (4-hydroxyphenyl) methanone 4.13(a-e), (3-(6-((2,3-diphenyl quinoxalin-6-yl) methyl) benzo[d] thiazol-2-yl amino) methyl) -4,5- dihydro -5- (4- substituted phenyl) pyrazol-1-yl) (4-chloro phenyl) methanone 4.14(a-e). 2-amino benzothiazole, (4.7) and 2,3 diphenyl quinoxaline, (4.8) were fused with methylene bridge. The formed product, 6-((2,3-diphenylquinoxalin-6-yl)methyl)benzo[d] thiazol-2-amine (4.9) was acetylated to give 1-(6-((2,3-diphenyl quinoxalin-6-yl) methyl) benzo[d] thiazol-2-ylamino) propan-2-one (4.10) and then the chalcones, (E)-1-(6-((2,3-diphenylquinoxalin-6-yl)methyl) benzo [d]thiazol-2-ylamino)-4-(4-substituted phenyl)but-3-en-2-one 4.11(a-e) were prepared using 5 different aldehydes. The formed chalcones were condensed with 3 different aromatic acid hydrazides to give 15 new benzothiazole pyrazolo quinoxaline compounds i.e., 4.12(a-e), 4.13(a-e), 4.14(a-e). They were purified and fully characterized based on their I.R, N.M.R and Mass spectral data.

CHAPTER-5: Antioxidant and Anti inflammatory screening of new quinoxaline compounds.

An introduction to oxidation, antioxidant activity, inflammation and anti-inflammatory activity was discussed at the beginning of this chapter. Then the methods used for antioxidant and anti-inflammatory studies were discussed.
For antioxidant study DPPH method (invitro) and ABTS (Invitro) free radical scavenging activity methods were followed and for anti-inflammatory study Carrageenan induced rat hind paw edema method (Invivo) was followed. All the synthesized 45 new quinoxaline compounds i.e., 15 new pyrazolo indoloquinoxaline compounds 2.12(a-e), 2.13(a-e), 2.14(a-e), 15 new benzimidazole pyrazolo quinoxaline compounds 3.12(a-e), 3.13 (a-e), 3.14(a-e) and 15 new benzothiazole pyrazolo quinoxaline compounds 4.12(a-e), 4.13 (a-e), 4.14(a-e) were screened for antioxidant study in three different sets for convenience. Ascorbic acid was taken as the standard drug in both invitro studies, and the % scavenging of free radicals was measured. The results after the screening were reported in this chapter.

Among the three different sets mentioned above, the compounds which showed better % scavenging of free radicals were selected for anti-inflammatory study. They were also screened in 3 different sets using Carrageenan induced rat hind paw edema method (Invivo) taking Ibuprofen as standard drug. The results after the screening were reported.

CHAPTER-6: Antihistaminic activity of new quinoxaline compounds.

An introduction to histamine and antihistamic agents, biological actions of histamines, distribution of histamine receptors, classification of H1 antihistaminic agents were discussed in the beginning of this chapter. Literature survey also revealed the diverse biological and
pharmacological significance of several nitrogen atom containing heterocyclic compounds. In view of the fact that benzimidazole, benzothiazole, quinoxaline and pyrazole moieties have potential H₁ antihistaminic activity, it has been considered worthwhile to evaluate the fused heterocyclic compounds synthesized in chapter 2, 3 and 4 for the H₁ antihistaminic activity.

For the antihistaminic study, Histamine chamber method (Invivo) was followed. Chlorpheneramine maleate was used as standard drug; good % protection against convulsions was measured. The experimental procedure and results were discussed.

CHAPTER-7: Antimicrobial screening of new quinoxaline compounds.

Among the antimicrobial studies we have selected antibacterial and antifungal screening of newly synthesized compounds. An introduction to antimicrobial agents, classification of antibacterial agents, types of bacteria, classification of antifungal agents was discussed at the beginning of this chapter.

All the new compounds synthesized in chapter 2, 3 and 4 were screened for antibacterial and antifungal activity respectively in 3 different sets for convenience. The experimental procedure and results were discussed.