Summary

The biological and pharmacological importance of quinoline fused linear and angular heterocycles containing oxygen, nitrogen and sulphur heteroatoms viz furo, pyrrolo, thieno and pyrano quinolines, we focussed our interest towards the synthesis of novel linearly and angularly fused quinoline heterocycles viz., 4-phenyl-furo[2,3-*b*]quinoline-2(3*H*)-one, 4-phenyl-furo[3,2-*c*]quinoline-2(3*H*)-one, 3-hydroxy-4-phenyl-furo[2,3-*b*]quinoline 3-hydroxy-4-phenyl-furo[3,2-*c*]quinoline, 3-hdydroxy-4-methyl-pyrrolo[2,3-*b*]quinoline, 3-hydroxy-4-phenylpyrrolo[2,3-*b*]quinoline, 3-hydroxy-4-phenyl-pyrrolo[3,2-*c*]quinoline, 3-hydroxy-4-phenylpyrrolo[2,3-*b*]quinoline, 4-methylthieno[2,3-*b*]quinoline-3(2*H*)-one, 4-phenyl thieno [2,3-*b*]quinoline-3(2*H*)-one, 4-phenylthieno[3,2-*c*]quinoline-3(2*H*)-one, 4-hydroxythieno [3,2-*c*]quinoline-3(2*H*)-one, 5-hydroxypyrano[4,3-*c*]quinoline-1,3(4*H*)-dione, 5-phenyl pyrano[3,4-*b*]quinoline-1,3(4*H*)-dione.

Precursors being the prior moiety to design the expected synthesis, we have synthesised the precursors 2-hydroxy-4-phenyl quinoline, 4-hydroxy-2-phenyl quinoline, 2-hydroxy-4-methyl quinoline, and 2,4-dichloro quinoline. Preparations of the starting compounds are discussed in appropriate chapters.

Chapter I dealt with the synthesis of linear and angular furo quinolin-2-one and linear and angular 3-hydroxy furo quinolines.

The precursors 2-hydroxy-4-phenyl quinoline and 4-hydroxy-2-phenylquinoline were obtained by the cyclisation of benzoyl acetanilide with H_2SO_4 and Polyphosphoric acid respectively.

2-hydroxy-4-phenyl quinoline underwent oxidative cyclisation with Chloro acetyl chloride in a single step, yielded linearly fused 4-phenylfuro[2,3-*b*]quinolin-2(3*H*)-one.

Following the same procedure, the precursor 4-hydroxy-2-phenylquinoline yielded angularly fused furo quinoline 4-phenylfuro[3,2-*c*]quinolin-2(3*H*)-one.

Chapter I also includes the synthesis of 3-hydroxy-4-phenylfuro[2,3-*b*]quinoline and 3-hydroxy-4-phenylfuro[3,2-*c*]quinoline from the 2- hydroxy-4-phenyl and 4-hydroxy-2-phenyl quinoline via their intermediates 4-phenyl-quinolin-2-oxo carboxy ester and 2-phenyl-quinolin-4-oxo carboxy ester by Dowtherm A respectively.

After achieving, the furo quinolines, synthesis of linearly and angularly fused Pyrrolo quinolines were attempted.

Chapter II describes the synthesis of linear and angular pyrrolo quinolin-3-ols.

The linear 3-hydroxy-4-methyl-pyrrolo[2,3-*b*]quinoline, 3-hydroxy-4-phenyl-pyrrolo [2,3-*b*]quinolines were synthesised from 2-hydroxy-4-methyl quinoline and 2-hydroxy-4-phenylquinoline respectively via their intermediates ethyl 4-methyl-quinolin-2amino carboxy ester and 4-phenyl-quinolin-2amino carboxy ester.

Chapter II concludes with the description of the synthesis of angularly fused 3-hydroxy-4-phenyl-pyrrolo[3,2-*c*]quinoline by the cyclisation of 2-phenylquinolin-4-amino carboxy ester.

Pharmacological importance of thieno quinolines, has implied the importance of the developing the newer thieno quinoline moieties. Hence in Chapter III we explained the synthesis of novel thieno quinolines.

Accordingly, first the reaction methodology involved in the synthesis of linearly fused thieno quinolines namely 4-methylthieno[2,3-*b*]quinolin-3(2*H*)-one, 4-phenylthieno [2,3-*b*]quinolin-3(2*H*)-one obtained from 2-hydoxy-4-methylquinoline and 2-hydoxy-4-phenylquinoline were explained.

4-methylthieno [2,3-*b*]quinolin-3(2*H*)-one was obtained from the dehydrohalogenation (K_2CO_3/DMF) of 4-methylquinolin-2-thio acetyl chloride which inturn was obtained by the action of thioglycolic acid and 2-chloro-4-methyl quinoline.

4-phenyl thieno[3,2-*c*]quinolin-3(2*H*)-one was obtained by the cyclisation of 4-phenylquinolin-2-thioaceticacid as an intermediate with PPA.

This chapter further describes the synthesis of angularly fused 4-phenylthieno[3,2-*c*] quinolin-3(2*H*)-one and 4-hydroxythieno[3,2-*c*]quinolin-3(2*H*)-one by reacting 4-chloro-2-phenyl and 4-chloro-2-hydroxyquinolines with thioglycolic acid followed by the usual workup procedure.

Being achieved various five membered heterocycles viz furo, Pyrrolo, thieno quinolines we extended our synthetic route towards six membered fused quinolines.

The synthesis of various substituted angular pyrano quinolines from 2-hydroxy-4-methyl quinoline via their intermediate 2-hydroxyquinolin-4-carboxy chloride.

Chapter IV includes the synthesis of various substituted novel angular pyrano quinoline-1,3-diones. For the synthesis of [4,3-*c*]pyrano quinolines were developed from the potential precursor 2-hydroxy-4-methylquinoline. The precursor, methyl substituted quinoline, was first converted into corresponding quinolin-4-carboxy chloride derivatives through quinolin-4-carboxylic acid.

5-hydrxypyrano[4,3-*c*]quinolin-1,3(4*H*)-dione has acquired from the intermediate 2-hydroxy quinolin-4-carboxy chloride by cycloaddition.

The hitherto novel linear and angular furo, pyrrolo, thieno, pyrano quinoline derivatives were synthesised. The intermediates formed and final products were confirmed with IR, ^{1}H-NMR, ^{13}C-NMR and Mass spectral data.

The **chapter V** compiles computational, pharmacological and photophysical studies of the novel synthesised compounds.

Quantum chemical descriptors, molecular electrostatic potential and first order hyperpolarizability of all synthesised compounds were calculated using DFT method with B3LYP/6-31G.

The *invitro* pharmacological activities of the selected synthesised compounds antimicrobial, antioxidant activities were discussed.

Furo, pyrrolo, thieno, pyrano quinolines were studied against three gram positive bacteria viz *Staphylococcus aureus*, *Streptococcus pyogenes*, *M.luteus*, four gram-negative bacteria viz *Pseudomonas sp, Escherichia coli, P.aeruginosa, K.pneumonia* and two pathogenic fungi viz *Aspergillus niger, C.albicans*.

The results obtained from the biological studies were correlated with the quantum chemical parameters.

The antioxidant activity of the selected synthesised compounds was studied their radical scavenging ability against DPPH.

The pharmacological activities of all the synthesised furo, pyrrolo, thieno, pyrano quinolines were significant.

The *in-silico* studies viz drug likeness, ADME, molecular docking and molecular dynamic simulation studies were carried out for some of the selected compounds.

C47B222 Fab Heavy Chain (**5TZ2**), histidine-rich glycoprotein(**4CCV**), Elastase 1(**2CV3**), Shikimate O-hydroxycinn Amoyl transferase(**5KJU**), DNA topoisomerase 2-alpha (**4FM9**), topoisomerase I DNA (**1A36**), DNA topoisomerase i(**1EJ9**), DNA(**2K4L**) and Zta transcription Factor(**5SZX**) were chosen and docked with furo, Pyrrolo and pyrano quinolines.

The photophysical properties were also envisaged in chapter V. NLO calculations, absorbance and fluorescence spectra and lifetime fluorescence studies for the selected compounds were calculated in order to evaluate their chemo sensor nature.

The theoretical aspects of the synthesised compounds are well in line with the experimental correlations.