Chapter 4
Plan of Study

4. PLAN OF STUDY

4.1 Design and synthesis of curcumin analogues

- ✓ Synthesis of hexahydroindazole analogues of curcumin
- ✓ Synthesis of pyrazole analogues of curcumin
- ✓ Synthesis of cycloheptanones analogues of curcumin

4.2. Characterization of synthesized compounds by using modern analytical tools viz.

- ✓ FT-IR, ^{1}H NMR, ^{13}C NMR and Mass Spectrometry

4.3. Evaluation of *in vitro* antimicrobial activity of synthesized compounds

Antimicrobial activity of newly synthesized compounds will be first screened by disc diffusion method against various Gram positive and Gram negative human pathogenic bacteria viz. *Escherichia coli* ATCC 25922, *Pseudomonas aeruginosa* ATCC 27893, S*almonella typhi* MTCC 3216, *Escherichia faecalis* and *Staphylococcus aureus* ATCC 25323 and different fungal strains of Candida according to the guidelines of National Committee for Clinical Laboratory Standards (NCCLS, 1997).

4.4. Molecular docking study of synthesized compounds against antimicrobial target Glucosamine-6-phosphate synthase

Automated docking will be used to determine the orientation of inhibitors bound to the active site of GlcN-6-P synthase. A genetic algorithm method, implemented in the program AutoDock4.2, will be employed. The 3D structure file of syntheised curcumin analogues and fluconazole molecule will be loaded on to PRODRG server and PreADMET server for energy minimization and drug likeliness prediction respectively. The protein structure file (PDB ID: 1JXA) will be downloaded from Protein Data Bank (www.rcsb.org/pdb).

4.5 Evaluation of *in vitro* anti-malarial activity of synthesized compounds

Anti-malarial activity of synthesized compounds will be evaluated against the multidrug resistant *P. falciparum* W2 strain (resistant to Chloroquine), using the method described by Makler *et al.* The parasites will be maintained in continuous *in vitro* culture and the quantitative assessment of *in vitro* anti-malarial activity will be determined by means of the microculture radio isotope technique.

4.6 Quantitative structure activity relationship (QSAR) study of synthesized compounds

Stepwise multiple linear regression analysis method will be used to perform QSAR analysis employing VALSTAT programme.