Chapter III  
SCOPE, OBJECTIVES AND PLAN OF WORK

Motivation

- Raising incidence of HIV related TB deaths which are exacerbated by drug resistance.
- Drug-drug interactions of combined drug therapy.
- Reduced patient compliance due to high pill burden.

Research Gaps

- Non availability of single drug therapy for the treatment for HIV/TB co-infection.
- Very limited number of piperidine-4-imines and its bis-arylidene derivatives (curcumin analogues) are available in the literature.
- The anti-tubercular and anti-HIV activities of these derivatives were not explored.

Objectives

The main objectives of the proposed research work were to:

- Design novel piperidone/piperidine derivatives using molecular docking methods.
- Determine the drug likeliness based on Lipinski’s and Veber’s rules
- Calculate the pKa value
- Synthesize the molecules, which were having good dock score.

- Characterize the synthesized piperidone derivatives using physical and spectral methods (IR, NMR and Mass).

- Carry out the antitubercular and anti-HIV activity (microbiological screening) using *in-vitro* cell based assay methods.

- Find out the interaction between the receptor and the synthesized molecules using molecular docking methods

**Importance of Proposed Research Investigation**

- In computational studies, some 3,5-bis arylidene substituted piperidones exhibited good oral bioavailability and good pharmacokinetic profile.

- Piperidone derivatives were designed to combat HIV/TB co-infection.

- Since curcumin has been reported to be extremely safe even at very high doses, we may expect the resulting compounds, the bisarylidene derivatives, with less or without any toxic effects.

- EACP reductase has been validated as an effective antimycobacterial target.

- Integrase is an attractive new class of anti-HIV drug targeting because of the absence of cross resistance and also synergism with other antiretroviral agents.
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PLAN OF WORK

I) DESIGNING OF MOLECULES

- Molecular Docking Study
  - Anti-TB
  - Anti-HIV

- Drug-Likeness
  - Lipinski's Rule of Five
  - Veber's Rule

II) SYNTHESIS

- 1-(1H-benzimidazol-2-ylmethyl)piperidin-4-substituted imines
- 1-(1H-benzimidazol-2-ylmethyl)-3,5-bis(furan-2-ylmethylidene)piperidin-4-substituted imines
- 3,5-bis(furan-2-ylmethylidene)piperidin-4-substituted imines

III) CHARACTERIZATION

- IR
- NMR
- MS
- EA

IV) IN-VITRO SCREENING

- Anti-TB
  - Agar dilution method
    - H37Rv Strain
  - Toxicity
  - MTT Assay
    - Vero Cell Lines
  - Anti-HIV
    - Single Cycle Assay
      - HIV-1 HXB2
    - Multi Cycle Assay
      - HIV-1 IIIB
    - Toxicity
      - XTT Assay
        - MT-2, TZM-bl