3 Objectives and plan of work

3.1 Objectives

1. To develop and characterize vinorelbine bitartrate loaded nano-formulations for treatment of breast cancer
    a. Solid lipid nanoparticles (PL-VRL-SLNs & TPGS-VRL-SLNs)
    b. Lipid based aqueous core nanocapsules (GMS-VRL-ACNs)
    c. Polymeric aqueous core nanocapsules (PLGA-VRL-ACNs)
2. To carry out in-vitro anticancer activity of VRL nano-formulations on MCF-7 cell lines
3. To evaluate prepared nano-formulations for safety following intravenous administration
4. To carry out synergistic drug combination studies for enhanced anticancer efficacy and dose reduction.
5. To develop and characterize dual drug loaded Aqueous core nanocapsules for drug combinations; PLGA-VRL+RES-ACNs and GMS-VRL+RES-ACNs
6. To evaluate in-vivo anticancer efficacy of dual drug loaded nanocapsules

In order to full-fill the above objectives, numerous formulations were fabricated and screened for the desired physicochemical properties, stability and *in-vitro* release kinetics. Selected formulations were taken up for *in-vitro* anticancer activity on MCF-7 cell lines. The results

of physico-chemical characterization and *in-vitro* release and cell line studies have been presented in this dissertation work

3.2 Detailed research plan

1. Analytical method development for simultaneous estimation of two drugs
2. Formulation Development
    - Solid lipid nanoparticles (TPGS-VRL-SLNs & PL-VRL-SLNs) by Solvent diffusion method and optimization by Taguchi optimization design.
    - Aqueous core nanocapsules (PLGA-VRL-ACNs & GMS-VRL-ACNs) by Double Emulsion Solvent Evaporation Method and optimization by Box Behnken design
    - Synergism analysis of ratiometric drug combination
    - Dual drug loaded ACNs (PLGA-VRL-RES-ACNs & GMS-VRL-RES-ACNs)
3. Characterization of prepared Nanoformulations
    - Particle size, PDI and Zeta potential
    - Entrapment Efficiency
    - SEM (Scanning Electron Microscopy)/TEM (Transmission Electron Microscopy)
    - Drug excipient compatibility studies
        - FTIR
        - DSC
    - *In-vitro* Release studies
    - Stability studies
4. *In-vitro* cytotoxicity
5. Intravenous safety assessment of nanoformulations
    - Haemolysis studies

- Platelet aggregation studies

6. *In-vivo* studies

   - Toxicity evaluation of developed formulations in Sprague dawley rats by Biochemical estimations
   - *In-vivo* anticancer efficacy of best formulation in Murine models