# 3 Research Envisage and Plan of Work

## 3.1 Aim

The present research work aimed at development, optimization, and characterization of two types of nano-colloidal micellar systems for loading and delivery of LP; (A) Polymeric micelles prepared from SOL, (B) Binary micelles fabricated by the combination of SOL and SHS.

## 3.2 Objective

The objective of the study was to assess the viability of PMs and BMs for improving solubility, stability, and encapsulation of highly hydrophobic anticancer drug, LP, and investigate their safety and efficacy for better treatment of HER2-positive breast cancer by conducting various *in-vitro* and *in-vivo* studies.

## 3.3 The rationale of a study:

Although LP is a potent chemotherapeutic agent, its poor solubility, encapsulation, and high dose limits its clinical use. It lacks patient compliance in terms of the high cost of therapy and also associated side effects. To date, only one type of its dosage form, i.e., tablet, is available in the market, which has to be administered at a high dose (1250 mg per dose). The above-said limitation might be due to its extreme poor aqueous solubility that does not increase by using generally used surfactant in the industry. So, It is the need of the hour to have some alternative dosage form of LP to circumvent the drawbacks of the available dosage form.

Thus, we developed Lapatinib-loaded nanocolloidal micelles and hypothesized that fabricated micelles would (i) encapsulate the drug with high drug loading and encapsulation efficiency (ii) release the drugs in a sustained and controlled manner, (iii)

enhance the therapeutic potential of drug bypassing hepatic metabolism, drug adsorption to the blood components (iv) their nanosize could target the tumors passively via EPR effect (v) enhance the anti-cancer efficacy of the drug at a lower dose (vi) reduce the dose-related toxicity of the drug and (vii) lower the total cost of treatment.

## 3.4 Plan of work

### 3.4.1 Preformulation studies

- HPLC method development and validation for the estimation of LP in *in-vitro* and *in-vivo* biological samples
- Physicochemical characterization of LP and excipients
- Determination of CMC of individual surfactant and their combination

### 3.4.2 Formulation development and optimization

- Screening of components for the formulation of micelles
- Optimization of micelles by Box-Behnken Design
- Formulation of LP-loaded micellar dispersion
- Lyophilization of LP-loaded micellar dispersion

### 3.4.3 Physicochemical characterization

- Particle size (PS) and polydispersity index (PDI) analysis
- Zeta potential determination
- Encapsulation efficiency (EE) and drug loading (DL) estimation
- Fourier Transform Infra-red (FT-IR) study
- Scanning Electron Microscopy (SEM) & Scanning Probe Microscopy (SPM) studies
- Energy Dispersive X-ray studies

- Stability Studies

### 3.4.4 *In-Vitro* evaluations

- Drug release studies
- Cytotoxicity studies
- Uptake studies
- Flow-cytometry analysis
- Hemolysis and platelet aggregation studies

### 3.4.5 *In-vivo* evaluations

- Pharmacokinetic studies
- *In-vivo* anticancer activity of dual drug-loaded formulations.
- Histopathological microscopy studies of liver tissues