CHAPTER 2

AIM AND OBJECTIVES OF THE STUDY

Camptothecin, quinoline alkaloid, showed potent anticancer activity against a wide range of cancers, including breast, lung, ovarian, pancreas and colon cancers (Pizzolato & Saltz 2003). Despite its higher cytotoxicity than its derivatives like topotecan and irinotecan, the clinical use of camptothecin is hampered due to its poor water and oil solubility; rapid conversion of active lactone form to less active carboxylate form at physiological pH and subsequent protein binding and rapid elimination from the body; and unpredictable severe non-target toxicity. Various camptothecin derivatives synthesized so far showed increased solubility and slightly enhanced bioavailability, but they also failed to overcome other problems associated with the parent compound (Patankar & Waterhouse 2012).

Several formulation approaches such as nanocrystalline suspension, solid lipid nanoparticles, micelles, liposomes, nanoparticles, microparticles, miniemulsions, dendritic polymers, prodrug approaches and drug-polymer conjugates had been attempted for delivering camptothecin and its derivatives by increasing their solubility and/or protecting the lactone ring hydrolysis in the physiological pH (Hatefi & Amsden 2002). But limited attempts were made to resolve other limitations (targeting, controlled release and toxicity) associated with camptothecin. Hence, an effective drug delivery system which keeps the lactone form of camptothecin intact, provides efficient targeting and predetermined controlled release of drug to the tumor tissue to prevent non-target toxicity is highly demanded.
In recent years, microemulsion (ME) has become one of the promising drug-delivery systems for the targeted delivery of poorly soluble drugs to the cancer tissue with enhanced bioavailability. The oil phase in the ME also serves as the reservoir for the lipophilic drugs and protects the drug molecule from the external physiological environment. Microemulsions/Nanoemulsions containing vincristine / curcumin are showed better drug accumulation at cancer tissue. (Junping W et al 2003, Jadhav et al 2006, Ganta & Amiji 2009).

Hence, the main objective of the present study was to develop and characterize the camptothecin loaded microemulsions, for passive/active targeted delivery to breast cancer tissues to achieve improvement in treatment.

The specific aims of this study were

I. Development of camptothecin loaded microemulsions and magnetic microemulsions using benzyl alcohol: captex 300 (3:1), TPGS (D-α-tocopheryl polyethylene glycol 1000 succinate):Tween 80 (1:2) and water for passive/active targeted delivery to BALB/c mice bearing breast cancer.

II. Formulation and characterization of camptothecin-loaded-polymer stabilized microemulsion (PSME) using capmul MCM: poloxamer 407 (4:1), solutol HS 15: simulsol P23 (1:2) and water for passive targeted delivery to BALB/c mice bearing breast cancer.

III. Evaluation of in-vivo passive/active targeting potential of developed microemulsions.

IV. Evaluation of in-vivo biodistribution and lactone ring stability of camptothecin in developed microemulsions.
Figure 2.1 Plan of work