OBJECTIVE OF THE PRESENT WORK

The vast majority of new chemical entities are neither peptides nor proteins, but molecules with a low molecular weight. It has been estimated that up to 40% of all new chemical entities show poor solubility (Straub et al., 2005). Particularly with the development of BCS class II and IV drugs with a low solubility and a low solubility and permeability respectively, which exhibit low oral bioavailability, companies are frequently faced with the choice to either develop or discard the early stage compound. In order to resolve this question, alternative delivery of technologies needs to be discussed and include in the early stages of drug development. For certain drugs that have a broad therapeutic window, require a low daily dose, and are going to be used for the long-term treatment of disease; injectable controlled release depots such as drug-loaded biodegradable polymer microparticles, nanoparticles may provide such an alternative delivery strategy, potentially rescuing an otherwise undeliverable drug.

Injectable microparticles from PLA and PLGA have been successfully prepared to deliver drugs like peptides, proteins, and vaccines over a period of days, weeks, or even months at a constant rate depending upon the degradation behavior of the polymer employed (Yeh M. K, 1996). However due to their large size, it was impossible to direct the drug to target tissues via systemic circulation or across the mucosal membrane (Brannon-Peppas L. 1995). Following oral administration, particles less than 500 nm can cross the M cells in the Payer's patch and the mesentery on the surface of the gastrointestinal mucosa, delivering the drug to the systemic circulation (Brannon-Peppas L. 1995). PLGA, a biodegradable and biocompatible polymer, has been extensively used for developing an array of microparticulate and Nanoparticulate drug delivery systems via injection and has several advantages, such as good mechanical properties, low immunogenicity, low toxicity, excellent biocompatibility, and predictable biodegradation kinetics. Effective immunosuppression is an essential pre-requisite for successful organ transplantation and improvements in outcome after transplantation have to a large extent been dependent on developments in immunosuppressive therapy. Corticosteroids are still widely considered an important component of most immunosuppressive regimens and are almost universally used as first-line treatment for acute allograft rejection. The two main corticosteroids used for the prevention of allograft rejection are prednisolone (used mainly in Europe) and prednisone (used mainly in the U.S.A.). In general, studies examining early withdrawal (within the first 3 months post transplant) have shown a higher incidence of acute rejection. In case
study, a total of 266 patients were randomized to continue prednisone at a dose of 10–15 mg/day or to have prednisone withdrawn over 8 weeks. The cumulative incidence of acute rejection was 30.8% for the steroid withdrawal group compared to 9.8% in those patients continuing steroids. Chitosan is a biodegradable natural polymer with great potential for pharmaceutical applications due to its biocompatibility, high charge density, non-toxicity and mucoadhesion. It has been shown that it not only improves the dissolution of poorly soluble drugs but also exerts a significant effect on fat metabolism in the body.

Hence the objective of present work is to develop, optimize and characterize Multiparticulate drug delivery system using biodegradable polymer for controlled release for drugs.

- To control release for drug, indicated for long-term treatment of disease (Immunosuppressant drug) and deliver it over a long period of time at a constant rate using biodegradable polymer.
- To improve the dissolution rate and bioavailability of poorly soluble drug (Anti-Migraine) by developing chitosan multiparticulate drug delivery.
- To implement “Quality by Design” approach to study effects of different formulation and process variables and optimize the design space for robust drug delivery system.