PREFACE

Nanotechnology is a growing technique in the pharmaceutical field and has been used extensively to circumvent the problems with existing delivery systems. These nanocarriers are targeted to the cancer cells by active or passive targeting to specifically act on the cancerous cells so that the toxicity to the normal cells can be averted. Paclitaxel (PTX), a naturally occurring diterpenoid isolated from Taxus bravifoliais a first line drug for the treatment of wide panel of solid tumors including urothelial, breast, lung and ovarian tumors. But it suffers from the disadvantage of poor water solubility and nonspecific biodistribution which causes serious side effects to the human body. Owing to its low water solubility, it was formulated in a mixture of cremophore EL and ethanol (50:50 %v/v), a marketed combination known as "Taxol" which suffers from serious side effects like allergic reactions, neutropenia, and neuropathy to the patients. Therefore it is the need of the hour to develop some alternative formulations of PTX which are free from cremophore EL. Genistein (Gen) (4', 5, 7-trihydroxyisoflavone) is a naturally occurring soy isoflavonoid, possessing anticancer, antiproliferation, antioxidant-like properties which makes it suitable to use as anticancer drug for the treatment of various cancers including genital and ovarian cancer. In spite of its strong antineoplastic activities, genistein somehow, did not find the place in the market due to its flaws for human use due to its less oral bioavailability. Therefore, the idea to work for the present thesis was envisaged from drug and dose-related problems of paclitaxel. In this perspective, the aim of the present study was to develop the nanoformulations (Lipid based nanostructured lipid carriers; NLCs & PLGA based polymeric nanoparticles) of Paclitaxel and Genistein and evaluate their potential for the treatment of ovarian cancer in combination, however PTX alone was also developed as NLC and polymeric nanoparticles and was evaluated

for all the parameters so that the toxicity and hypersensitivity reactions caused by paclitaxel can be prevented. We hypothesized that by combination of phytoestrogen (Gen) with the semisynthetic drug (PTX), as the dose of PTX will be reduced, the dose related toxicity will be reduced further due to sustained release potential of developed formulation, dosing frequency and total dose needed of PTX will be reduced, thus will result in safe and economic treatment of ovarian cancer. In pre formulation studies, HPLC based method was developed for the assay of individual drugs as well as for their combination that will be needed for the analysis of in vitro and in vivo samples. The ratiometric drug combination studies were carried out to determine the synergistic drug combination of Gen and PTX. Further, the formulation study was divided into 2 parts: Nanostructured lipid carriers (NLCs) of PTX, Gen and their combination and PLGA based polymeric nanoparticles of PTX, Gen and their combination. NLCs were formulated by Emulsification solvent evaporation technique and Polymeric nanoparticles were formulated by nanoprecipitation technique. Response surface methodology based Box Behnken design followed by desirability based numerical optimization technique was utilized for the optimization studies. The optimized nanoformulations were evaluated for various parameters like particle size, surface charge, morphology, entrapment efficiency, drug-excipient interaction, drug release studies, stability studies, cytotoxicity, evaluation of haemolysis, platelets aggregation, pharmacokinetic studies, *in vivo* anticancer activity & biochemical estimations. All these characteristics of newly designed nanoformulation system demonstrated it as a promising delivery system for the improved and safe treatment of ovarian cancer.