Literature Review:

Wong HL, Rauth AM, et.al, (2007) studied passive targeting of capecitabine nanoparticles in tumor bearing rats. The study revealed that polymers having hydrophobic moiety in the molecule such as are suitable material for the process of targeting and site specify delivery with absolute accuracy can be achieved by attaching bioactive molecule to nanoparticulate drug delivery system.


Gabrielle Pilcer, Francis Vanderbist, et al, [2009] demonstrated the possibility of delivering formulations to the lungs that are made up of a mixture of nano- and microparticles of the active drug. On the one hand, nanoparticles were used to coat micron-size particles and on the other hand, formulations composed of solely nanoparticles were produced in order to form easily dispersible and reproducible micron-size agglomerates of particles. These new carrier-free dry powders, with only a small amount of surfactant, present high lung deposition properties.

Bloomston M, Bhardwaj A, et.al, (2006) investigated targeted gene delivery system and can mediate efficient targeting of epidermal growth factor receptor expression in pancreatic carcinoma using tissue microarray technique.

Sachin K. Singh, Srinivasan K.K., et.al, [2010] studied, that polymer concentration ratio of polymer to drug and milling speed play a significant role in controlling the zeta potential of nanosuspensions. The study also helped in identifying certain formulation and processing parameters, such as high polymer concentration and high milling speed, which may affects the manufacturing of nanosuspension at higher scale.

Lei Gao and Dianrui Zhang [2007] studied, that formulation of ORI as a nanocrystal suspension has exhibited great success in dissolution rate and saturation solubility enhancement due to its size and enormous surface area. The HPH method was shown to be a simple and efficient technique for particle size reduction with the help of optimized stabilizers.

Eloubeidi MA, Russo S, et.al, (2005) studied on transporting efficiency of anti-cancer drugs, anti-bacterials or anti-fungals in nanoparticulate drug delivery system. The results revealed that nanoparticles can be successfully used as a non-viral vehicle for reaching targeted cells when performing gene therapy, and as antigen carriers for immunization.

Ji-Yeun Choi, Chul Ho Park, et.al, [2008] showed that itraconazole and hydroxypropyl cellulose were used to study the effect of the molecular weight of a polymer on particle size reduction. In principle, an increase in molecular weight produces two counteracting effects: a decrease in the diffusion rate of chains and an increase in the physical adsorption of a polymer. Based on the results of our research, it appears that polymers of smaller molecular weight are more suitable than larger polymers for efficient nanocomminution. This indicates that the kinetic aspects of molecular weight are important.

Kulke MH, Blaszkowsky LS, et.al, (2007) investigated the use of capecitabine nanoparticles in management of various solid malignancies. The study revealed that capecitabine nanoparticles can be used in colorectal cancer, breast cancer and various other tumor types.

Spomenka Simovic, He Hui, et.al.[2010] demonstrated that the physico-chemical and biopharmaceutical properties of a new class of hybrid lipid–silica microcapsules that contain poorly soluble and weakly acidic drug (indomethacin) that electrostatically interacts with oleylamine (cationic lipid present as stabilizer). Microcapsules are based on Pickering emulsions as the initial templates and were fabricated by either spray drying or phase coacervation.

Sudhir Verma, Diane J. Burgess, et.al.[2009], studied on Quality by design (QbD) principles were explored to maximize the understanding of the unit operation of microfluidization, for the preparation of nanosuspensions using indomethacin as a model drug. In order of importance, milling time, microfluidization pressure, stabilizer type,
temperature and stabilizer concentration were identified as critical parameters affecting the formation and stability of nanosuspensions. Interaction between homogenization pressure, temperature and milling time also significantly affected the nanosuspension particle size.

- **Leena Peltonen, Johanna Aitta et al. (2004)** demonstrated the entrapment efficiency of a model hydrophilic drug substance, sodium cromoglycate, loaded inside polylactic acid nanoparticles by a modified nanoprecipitation method. The entrapment efficiency was modified by changes in the solvent selection, the amount of the model drug substance (sodium cromoglycate), solvent selection, the pH values of the outer and inner phases, and, finally, by the addition of salt to the aqueous phases. The stability of the drug substance after the most successful drug loadings was studied by x-ray diffraction methods.

- **Andres R, Mayordomo J et al., (2005)** studied on Gemcitabine/capecitabine in patients with metastatic breast cancer pretreated with anthracyclines and taxanes and also in advanced pancreatic carcinoma.

- **Vijaykumar Nekkanti, Raviraj Pillai et al., [2009]** indicated that wet bead milling process coupled with spray drying is a viable approach for developing a nanoparticle formulation of candesartan that provided enhanced drug solubility and dissolution. Enhancing dissolution rate correlates with faster absorption, improved bioavailability with reduced variability that could translate into improved therapeutic outcome.

- **Suzanne M. Robert K. et al, [2010]** reviewed on nucleation and growth of organic nanoparticles at high supersaturation. We present process considerations for controlling supersaturations as well as physical and chemical routes for modifying API solubility to optimize supersaturation and control particle size. We conclude with a discussion of post precipitation factors which influence nanoparticle stability and efficacy in vivo and techniques for stabilization.

- **Mittal V.V., Patel S.J. et al,[2010]** developed and characterized tumor selective folate conjugated PEG(Polyethylene glycol) polymeric nanoparticulate system for paclitaxel delivery. Paclitaxel -loaded poly (lactic-co-glycolic acid) (PLGA) nanoparticles were prepared by the solvent evaporation method and characterized by scanning electron microscopy (SEM), atomic force microscopy (AFM) and zeta potential measurements.

- **Grau M.J., Kayser, O. et al,[2000]** studied milling process by high pressure
homogenization for the production of drug nanoparticles is highly reproducible with regard to the mean size and width of the distribution of the bulk population. In this report reproducibility of small scale production parameters (particle size, size distribution, and content of microparticles) was exemplary studied for the drug RMKP22.

- **Tangri, P. Khurana S. et al [2011]** reviewed on formulation approaches of nanoparticles and the potential use in the cancer therapy. It includes monolithic nanoparticles in which the drug is adsorbed, dissolved, or dispersed throughout the matrix and nanocapsules in which the drug is confined to an aqueous or oily core surrounded by a shell-like wall. Alternatively, the drug can be covalently attached to the surface or into the matrix. This review deals with the formulation approaches of nanoparticles and the potential use in the cancer therapy.

- **Kalle Sigfridsson and Sara Forssen [2007]** studied to find out if the three different formulations were comparable and safe to administer. The results indicate that AZ68 is absorbed at a lower rate for crystalline nanosuspensions compared to amorphous nanosuspensions and solution.

- **Kassema MA, and Abdel Rahman AA. [2007]** confirmed that nanosuspensions differ from micro-crystalline suspensions and solution as ophthalmic drug delivery systems and that the differences are statistically, highly to very highly significant. The effect of particle size in the micron and nano-size ranges as well as the effect of viscosity of the nanosuspension on the ocular bioavailability was studied the results show that compared to solution and micro-crystalline suspensions it is a common feature of the three drugs that the nanosuspensions always enhance the rate and extent of ophthalmic drug absorption as well as the intensity of drug action.

- **G. Maruthi G., Smith et al [2011]** reviewed various aspects of nanoparticle formulation, characterization, effect of their characteristics and their applications in delivery of drug molecules and therapeutic genes Cancer nanotechnology.

- **Lai F., Pini, E Angioni. G. et al [2010]**, prepared orally disintegrating tablets (ODT) using nanocrystal formulations in order to optimise dissolution properties of lipophilic, poorly soluble drug piroxicam (PRX). Different nanocrystal formulations et al prepared using a high pressure homogenisation technique and poloxamer 188 as Stabilizer; et.al concluded that the improvement in PRX dissolution rate is mainly caused by the increased surface-to-volume ratio due to the submicron dimension of the drug particles.
Patrice Tewa-Tagne, Stephanie Brianc on et al. [2007], studied, that the spray-drying technique interesting alternative to lyophilization in order to transform NC dispersions into a dry product. To date, little attention has been paid for the use of the spray-drying process to prepare redispersible spray-dried NC. et al investigating the possibility to stabilise NC within soluble MP designed to further disintegration in aqueous medium and reconstitution of NC dispersions.

Katy Margulis-Goshen, MSc, et al. [2009], studied, a new method to prepare nanoparticles of a poorly water-soluble drug, simvastatin, by evaporation of all solvents from spontaneously formed oil-in-water microemulsions. Tablets containing the flakes of Simvastatin nanoparticles showed tremendous enhancement in dissolution profile compared with conventional tablets.

Wei Li, Yong gang Yang RH, et al. [2010] prepared nanosuspension and microsuspension by high pressure homogenization. Their crystalline state were evaluated by DSC and PXRD, and both evaluations indicated lattice energy of drug particles decreased with decrease of particle size, et al. shown that particle size reduction could increase RH in vitro dissolution rate. The smaller the particle size, the higher the dissolution rate.

XueMing Li, Li Gu et al. [2009,] improved the dissolution rate and bioavailability of lipophilic of fenofibrate by nanosuspensions with melt emulsification method combined with high-pressure homogenization was adapted, and mixture of poloxamer188 and PVP K30 were selected as surfactants. The dissolution rate of fenofibrate nanosuspension was increased obviously, and the product was evaluated by pharmacokinetic characteristic in rats. The AUC0–36 h and Cmax of nanosuspensions were increased when compared with the reference formulations.

Patel VV., Sheth SJ et al. [2010], studied to develop and characterize tumor selective folate conjugated PEG (Polyethylene glycol) polymeric nanoparticulate system for paclitaxel delivery. Paclitaxel-loaded poly (lactic-co-glycolic acid) (PLGA) nanoparticles were prepared by the solvent evaporation method and characterized by scanning electron microscopy (SEM), atomic force microscopy (AFM) and zeta potential measurements.

Harivardhan Reddy and R.S.R, Murthy. [2005]. prepared etoposide-loaded nanoparticles with glyceride lipids and then characterize and evaluate the in vitro steric stability and drug release characteristics and stability, et al. investigates the formation of
lipid nanoparticles by melt emulsification and a high-pressure homogenization technique followed by spray drying of the nanodispersion. Factors influencing the nanoparticles formation and spray-drying process were determined and optimized. The nanoparticles were subjected to electrolyte induced flocculation test to determine their steric repulsion properties.

> V. Jannin, J. Musakhanian, D. Marchaud et al [2008], reviewed in Lipid Based Drug Delivery (LBDD) has developed over the past decade fuelled by a better understanding of the multiple roles lipids may play in enhancing oral bioavailability, et al reviewed the recent approaches in selecting the most appropriate lipid system(s); methods for characterization of their behavior in vitro and in vivo; and the current formulation and processing techniques to obtain various solid dosage forms.