DEVELOPMENT OF LIPID NANOPARTICULATE SYSTEMS OF ANTI-CANCER AGENT FOR THE TREAMENT OF LUNG CANCER

P-055

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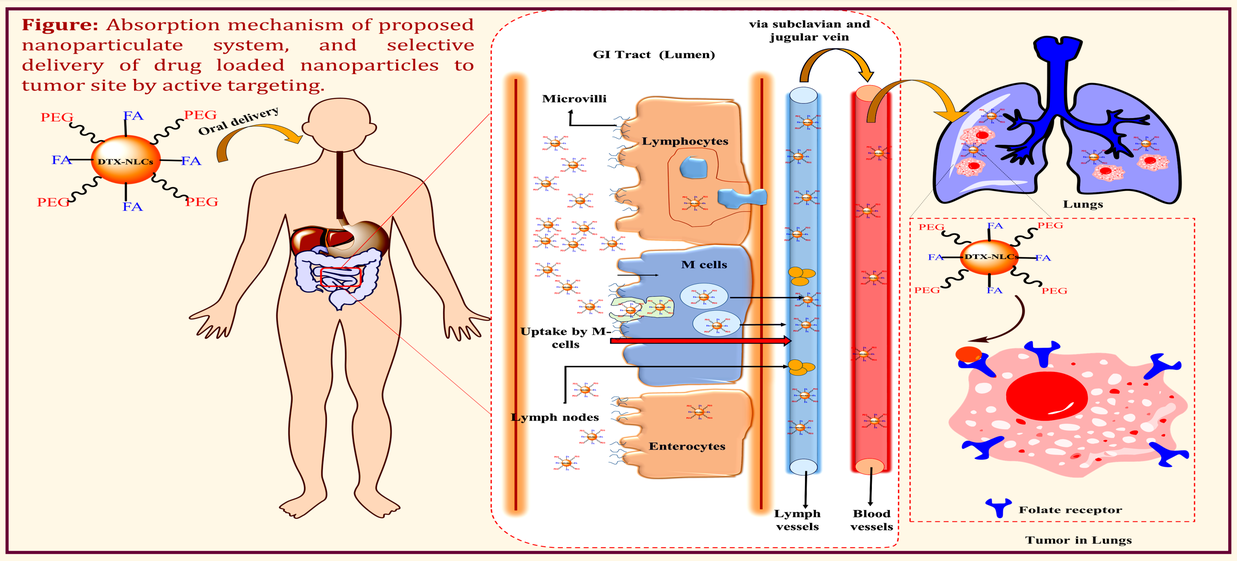
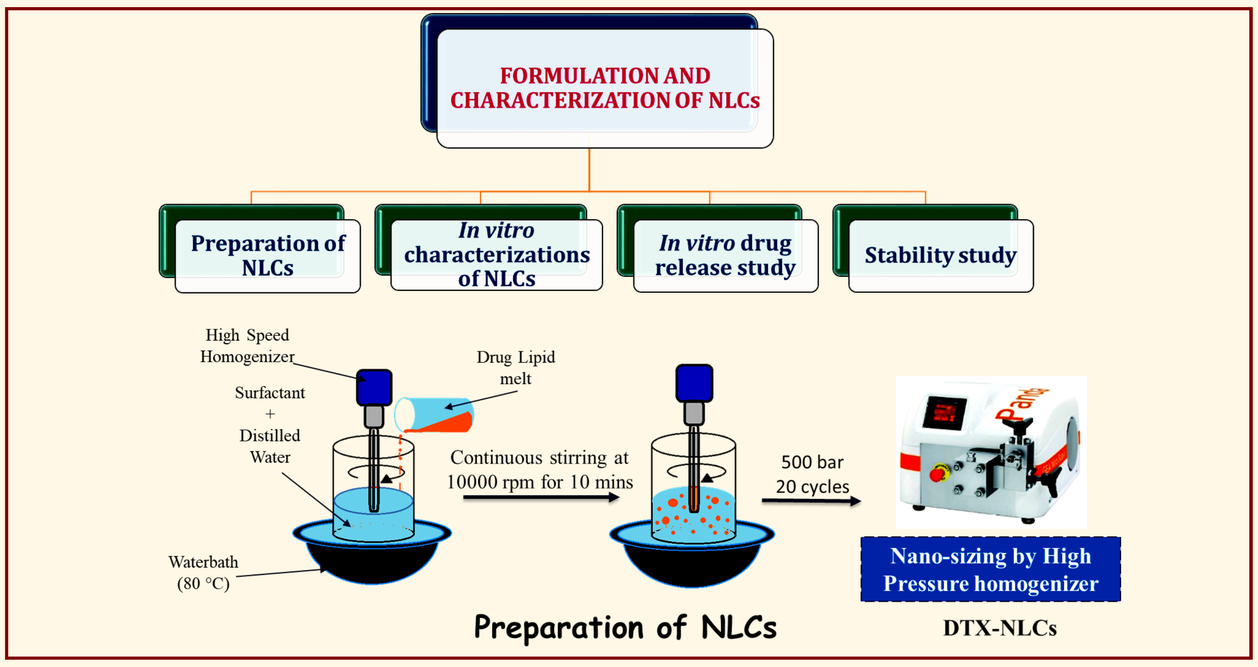
INTRODUCTION

- Lung cancer is the leading cause of cancer-related death in both men and women worldwide with a staggering 28% of total cancer death in United States alone.
- In India, lung cancer constitutes 6.9 per cent of all new cancer cases and 9.3 per cent of all cancer related deaths in both sexes, it is the commonest cancer and cause of cancer related mortality in men.
- Chemotherapeutical treatment generally includes administration of drug formulations mostly by intravenous route, which is painful, toxic, time consuming and costly for the patients.
- Chemotherapy also causes toxicity and cell death to other normal cells in the body apart from cancerous cells.
- The aim of the present investigation was to develop an orally administrable ligand appended docetaxel loaded PEGylated Nanostructured Lipid Carriers (DTX-NLCs) system.

Figure: Absorption mechanism of proposed nanoparticulate system, and selective delivery of drug loaded nanoparticles to tumor site by active targeting.





Evaluation of Significant factors

Concentration of drug mainly affects the %EE

Concentration of emulsifier was found to have greater impact on particle size and %EE

Homogenization Speed showed greater impact on particle size

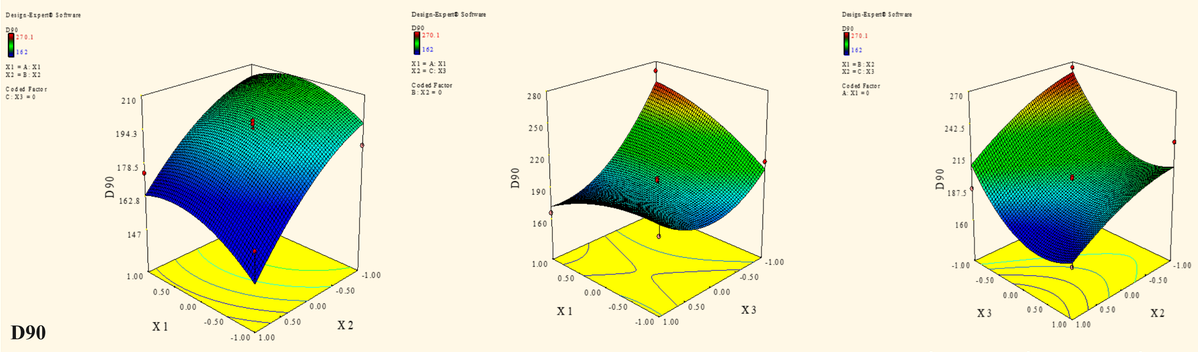
Independent Variables	Levels		
	-1	0	+1
X_1 = Amount of Drug (mg)	10	20	30
X_2 = Concentration of Emulsifier (%)	10	15	20
X_3 = Stirring Speed (RPM)	10K	12.5K	15K
Dependent variables	**Constraints**		
Y_1= D90 (nm)	Minimum		
Y_2= Z-avg. (nm)	Minimum		
Y_3= % EE	Maximum		

Box-Behnken Design

Batches	Factor			Independent variables		
	X_1	X_2	X_3	X_1	X_2	X_3
SS1	-1	-1	0	10	10	12.5K
SS2	+1	-1	0	30	10	12.5K
SS3	-1	+1	0	10	20	12.5K
SS4	+1	+1	0	30	20	12.5K
SS5	-1	0	-1	10	15	10K
SS6	+1	0	-1	30	15	10K
SS7	-1	0	+1	10	15	15K
SS8	+1	0	+1	30	15	15K
SS9	0	-1	-1	20	10	10K
SS10	0	+1	-1	20	20	10K
SS11	0	-1	+1	20	10	15K
SS12	0	+1	+1	20	20	15K
SS13	0	0	0	20	15	12.5K
SS14	0	0	0	20	15	12.5K
SS15	0	0	0	20	15	12.5K
SS16	0	0	0	20	15	12.5K
SS17	0	0	0	20	15	12.5K
SS18*	0	-0.5	0.5	20	12.5	13.75K
SS19*	-0.5	0	0.5	15	15	13.75K

*Check point batches

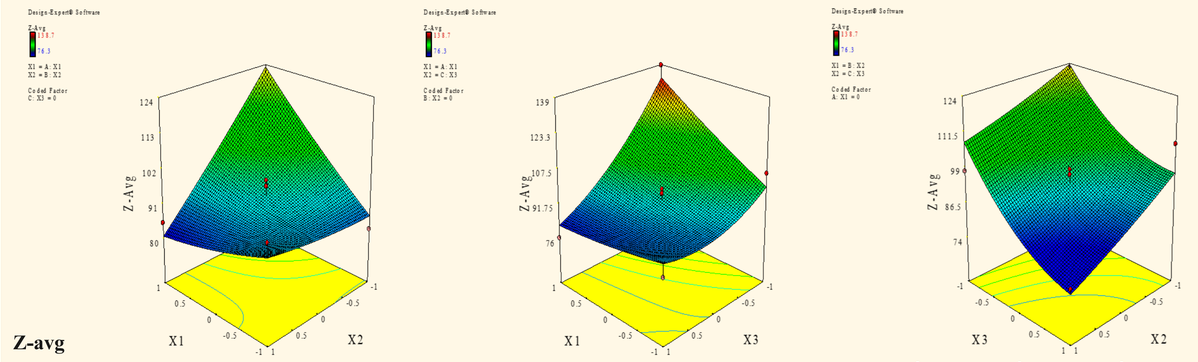
EFFECT OF INDEPENDENT VARIABLES ON DEPENDENT VARIABLES



D90

$Y_1 = +194.50 +5.81 * X_1 -22.41 * X_2 -23.20 * X_3 +2.27 * X_1 * X_2 -20.40 * X_1 * X_3 +3.65 * X_2 * X_3 -8.81 * X_1^2 -7.46 * X_2^2 +24.51 * X_3^2$

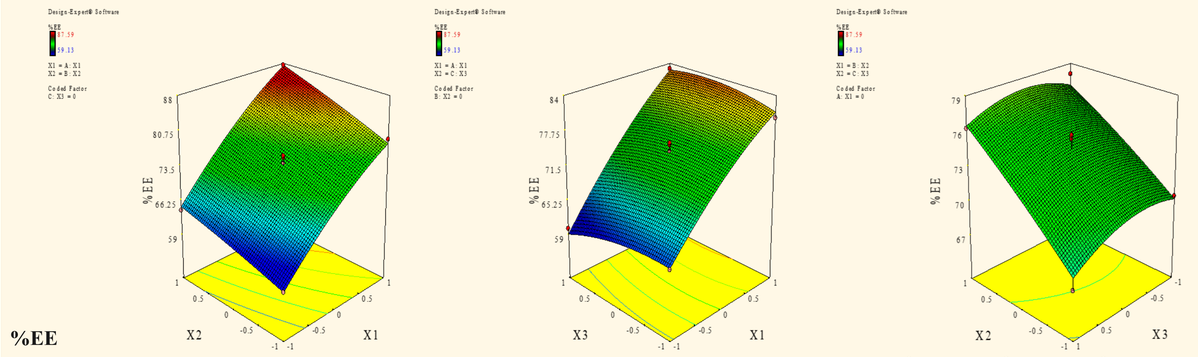
$R^2 = 0.8764$



Z-avg

$Y_2 = +93.64 +6.35 * X_1 -9.50 * X_2 -14.98 * X_3 -11.73 * X_1 * X_2 -10.33 * X_1 * X_3 -1.78 * X_2 * X_3 +1.14 * X_1^2 +0.89 * X_2^2 +6.39 * X_3^2$

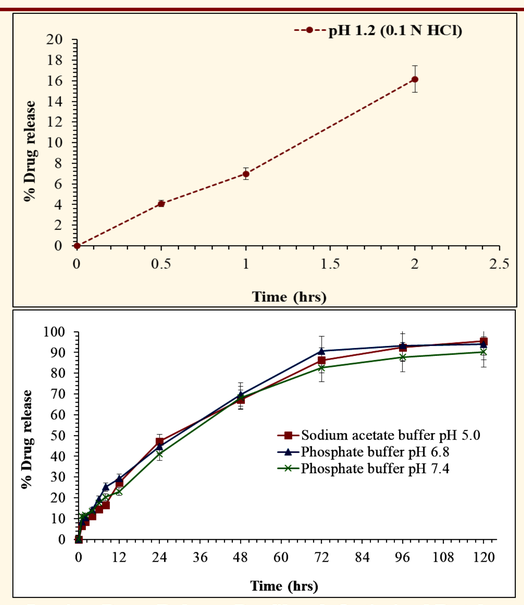
$R^2 = 0.8928$



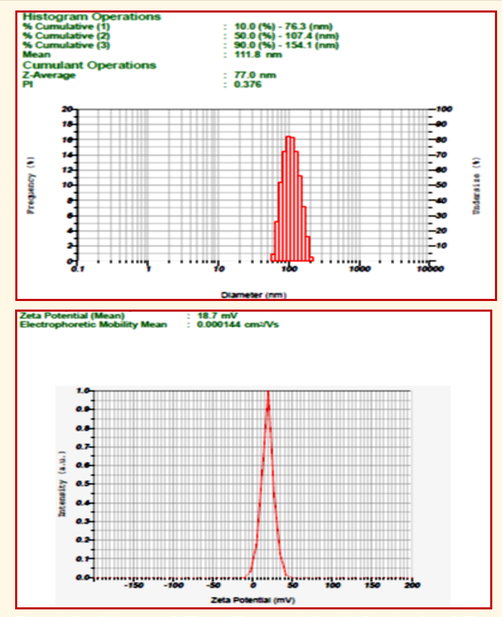
%EE

$Y_3 = +74.51 +10.43 * X_1 +3.79 * X_2 -0.61 * X_3 +0.85 * X_1 * X_2 +1.42 * X_1 * X_3 +0.36 * X_2 * X_3 -1.73 * X_1^2 -0.27 * X_2^2 -1.28 * X_3^2$

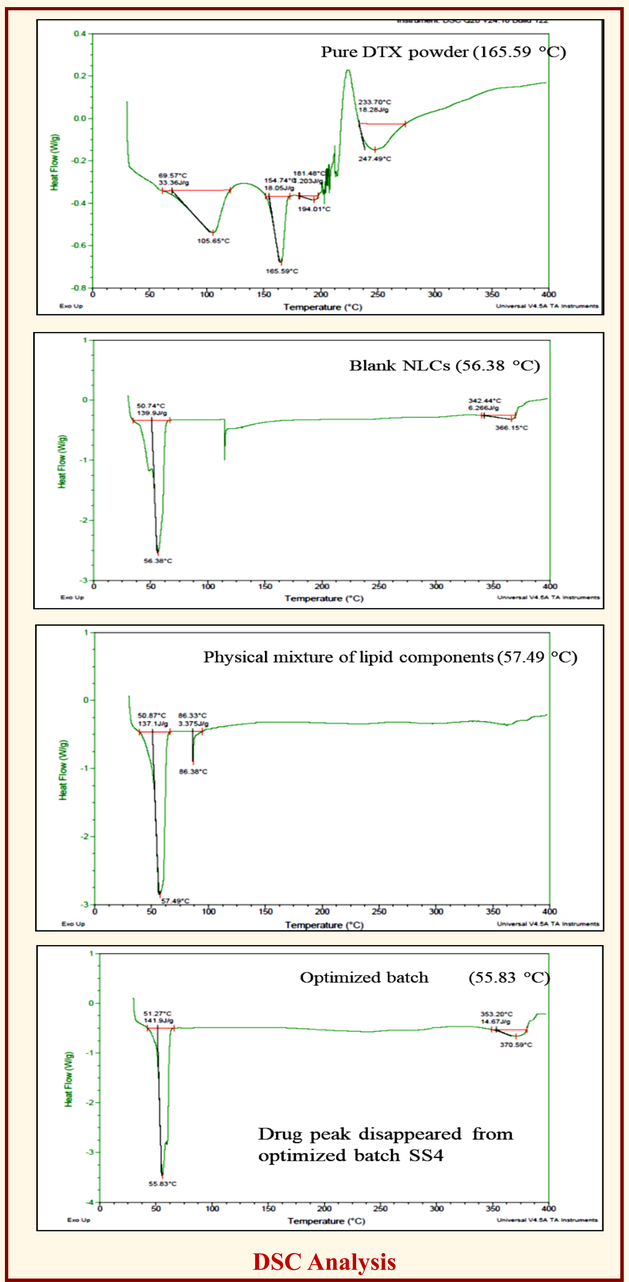
$R^2 = 0.9909$



***In-vitro* Drug Release Profile of Optimized Batch**

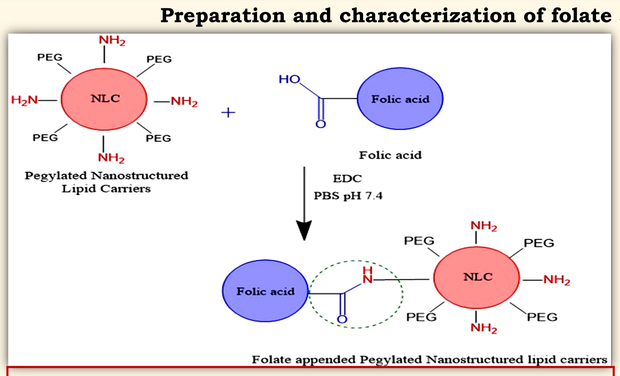


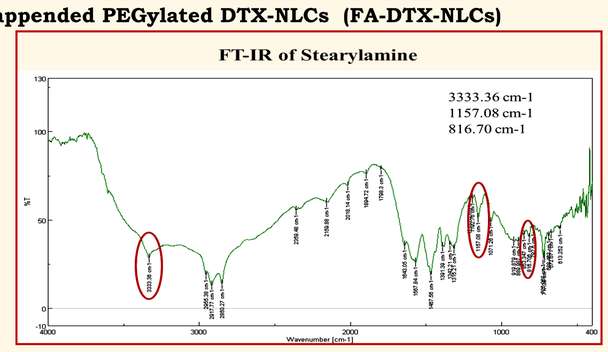
Particle Size and Zeta Potential of Optimized Batch

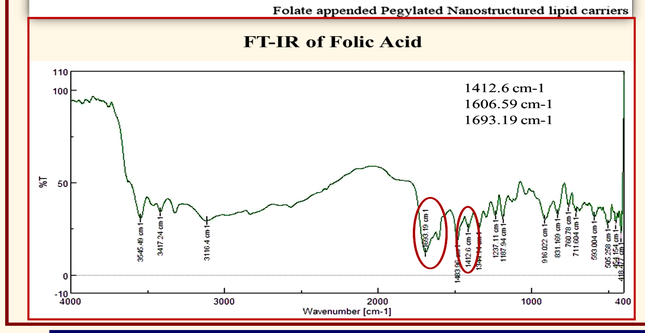


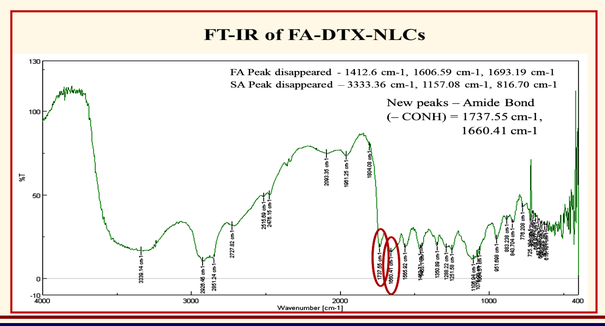
DSC Analysis

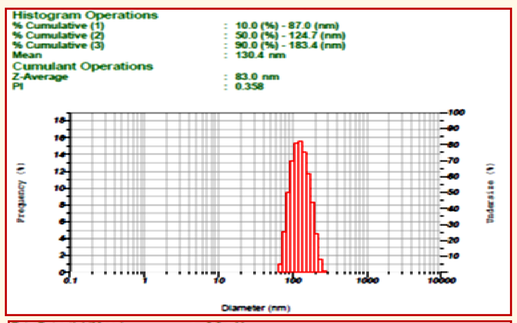
Preparation and characterization of folate appended PEGylated DTX-NLCs (FA-DTX-NLCs)

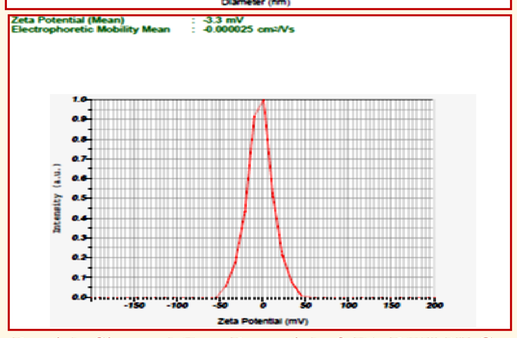




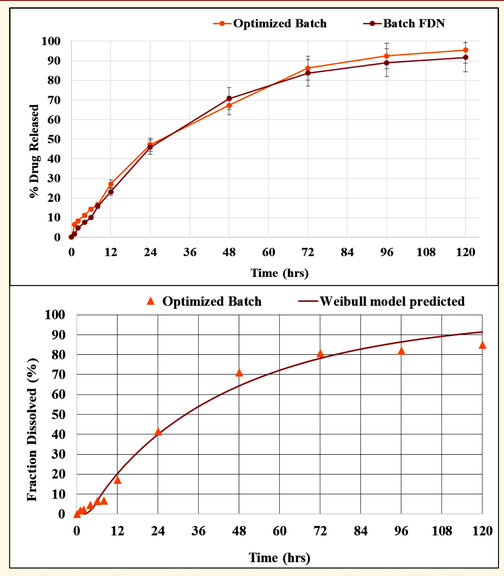








Particle Size and Zeta Potential of FA-DTX-NLCs



***In-vitro* Drug Release Profile of FA-DTX-NLCs**

REFERENCES

(1) Zhang L, Zhang N. Int J Nanomedicine 2013; 8: 2927-41. (2.) Tan Q, Liu X, Fu X, Li Q, Dou J, Zhai G. Expert Opin Drug Deliv 2012; 9(8): 975–90. (3) Goren D, Horowitz AT, Tzemach D, Tarshish M, Zalipsky S, Gabizon A. Clin Cancer Res 2000, 6:1949. (4) Leamon CP, Reddy JA. Adv Drug Delivery Rev 2004, 56:1127.

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