Formulation and Optimization of Silibinin loaded Inhalable liposomal nanoparticle for the treatment of Lung cancer.

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Abstract

The purpose of the present research work was to optimize Silibinin loaded liposomal nanoparticles using Rotary Evaporator followed Extruder technique by using QbD approach. Silibinin-loaded liposomal nanoparticles were conjugated with folic acid would increase the affinity of nanoparticles for cancer cells. Based on the risk assessment, variables, that is Cholesterol to lipid ratio, Volume of Organic solvent and Water Bath temperature were studied on critical quality attributes (CQAs) such as particle size, entrapment efficiency and drug release rate. Box Behenken design (BBD) was implemented for design of experimentation with 15 runs. Nanoparticles were characterized for particle size, polydispersity index, entrapment efficiency, in-vitro release study, DSC, FTIR, X-ray diffraction, scanning electron microscopy (SEM). Folic acid linkage was confirmed by NMR and FTIR study. *In vivo* study was performed in NNK induced lung cancer model. Design space was optimized based on the QbD approach, with a combination of selected variables with entrapment efficiency > 40% w/w and a particle size between 200 and 400 nm and drug release > 80% in 12 Hr. Validation of model was performed with check point batches from Design Space. Lower magnitude of standard error between observed value and predicted value for CQAs confirms the validation of selected model for optimization of prepared nanoparticles. *In vivo* study shows higher efficiency in drug delivery in the lung by inhalation route. Silibinin loaded chitosan nanoparticles were prepared successfully using QbD approach with the understanding of the high risk process and formulation parameters which are affecting on quality of formulations. This delivery platform can effectively facilitate targeting to human lung cancer cell lines in a sustained manner and so improve the therapeutic efficacy.