Summary: Conclusively, the present research work was aimed to design development and characterization of PTX and Gen based nanoformulations for the safe, effective and economic treatment of ovarian cancers. A sensitive, rapid, and precise HPLC analytical method was developed and validated for the estimation of PTX, Gen and their combination. Nanostructured lipid carriers (NLCs) of PTX, Gen and their combination were formulated by Emulsification solvent evaporation technique and polymeric nanoparticles of Gen, PTX and their combination were formulated by nanoprecipitation technique. Screening of process and product variables for the formulation of NLCs was done with Placket Burman design which was followed by Box Behnken Design while for polymeric nanoparticles, only Box Behnken design was utilized. Optimization of the formulations was done with desirability function based numerical optimization technique. The implementation of this multivariate statistical experimental design in formulation process provided stable, optimized nanoparticle after a profound understanding of the inherent relationship between formulation variables and the desired responses. The desired range of particle size, zeta potential, PDI and entrapment efficiency were obtained by using the range of factors indicated in the design. Morphological studies demonstrated smooth and spherical shape of the nanoparticles without any aggregation. Solid state characterization studies (FTIR, DSC and PXRD) concluded that there were no interactions between the drug and the respective excipients. The prepared formulations were found to be stable for sufficient period of time. Drug release profiles of the formulations in comparison to their pure drugs confirmed the prolonged release of the formulations which was further confirmed by higher plasma drug levels maintained for longer duration of time during pharmacokinetic studies. In vitro cytotoxicity was conducted using PA-1 human ovarian

cancer cell lines which confirmed viable cell reduction and indicated that % inhibition was much higher when treated with nanoparticles in comparison to pure drug suspensions. Heamolysis and platelet aggregation studies confirmed the suitability of the prepared nanoparticles for intravenous administration. Further, the in vivo efficacy studies of the nanoparticles containing combination of the drug were conducted on female Balb/C mice grafted with ID-8 murine epithelial ovarian cancer cells which the parameters like safety (survival) and efficacy (relative tumor volume data) were evaluated. Out of the prepared formulations, A3 formulation (PTX +Gen loaded NLCs) was found to be equally effective to the standard (Docetaxel,i.v) and less toxic in comparison to its pure drugs.

Conclusion: The strategy of inclusion of nanotechnology to the semi synthetic and phytoestrogen entity not only enhanced the chemotherapeutic potential of the individual drugs but also reduced its associated toxicities observed during conventional treatment. Further the inclusion of ratiometric combination of PTX and Gen (5:1) into the lipid as well as polymeric matrix resulted in synergistic effect which further reduced the dose of PTX thereby the dose related toxicity was minimized and had made the therapy safe & economic. All these characteristics of newly designed system demonstrated to be a promising delivery system for the combination therapy for the safe & economic treatment of ovarian cancer. Paclitaxel as well as Genistein were successfully entrapped into lipid core as well as polymeric matrix of nanoparticles and NLCs. However, dual drug loaded NLCs (A3 formulation) had smaller particle size and better anticancer activity with lower IC_{50} values, as compared to dual drug loaded polymeric nanoparticles. Thus, A3 formulation (PTX+Gen NLCs) can be considered as potential formulation for the treatment of ovarian cancer.

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