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## Lipid drug conjugated nanoparticles for the oral delivery of an Antifolate drug

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The aim of this study was to design and develop Lipid drug conjugated (LDC) nanoparticles for the oral delivery of Pemetrexed as an anitfolate agent for cancer therapy. LDC was produced using cold homogenization technique and was further characterized by various parameters; Particle size, Zeta potential, TEM, DSC, FTIR, AFM and XRD. Moreover, efficacy of the LDC towards the cancer cells was studied by ex vivo gut permeation study, CLSM, and MTT assay. The particle size of the optimized LDC was found to be 121.9 $\pm$ 0.787nm and Zeta potential of -51.6mV $\pm$ 1.23 indicating a stable formulation. Entrapment efficiency was found to be 81.0% $\pm$ 0.89. TEM images revealed spherical morphology and were in corroboration with particle size measurements. FTIR analysis of LDC proved the presence of amide bond in lipid drug conjugate powder indicating the conjugation between drug and lipid. XRD data had showed the reduced intensity of drug and lipid peaks. *In vitro* release kinetics indicated the sustained release behavior of the LDC with r2 value of 0.986 for first order release kinetics. Stability studies proved that the formulation was stable with shelf life of 777.134 days. Ex vivo gut permeation studies revealed a very good enhancement in permeation of drug present in the LDC as compared to plain drug solution and were confirmed by CLSM. MTT assay conformed significant % toxicity at the end of 24 hrs and 48 hrs. The pharmacokinetic data revealed that the LDC (AUC 6345.67 $\pm$ 9.47 h/mL) significant enhancement in the oral bioavailability as compared to plain drug solution (AUC 1501.02 $\pm$ 12.67 h/mL).

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