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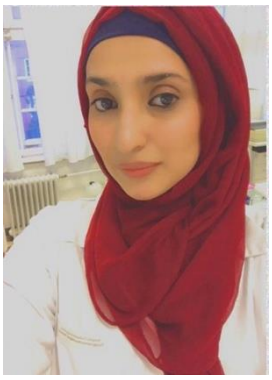

Nose to brain delivery of *n*-propylgallte loaded lipid nanoparticles for targeting glioblastoma multiforme via QbD approach

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This study aimed to develop liposomes and solid lipid nanoparticles (SLNs) encapsulated with *n*-propylgallate (PG) as potential platforms for nose-to-brain delivery of anticancer drugs. The lipid formulation loaded with PG was not studied previously through this administration route, therefore its investigation and optimization is promising. The liposomes, solid lipid nanoparticles were developed by direct pouring method and solvent injection method respectively following the Quality by Design approach. The risk assessment strategy was used to screen and rank the critical quality attributes that can affect the final PG loaded nanoparticles. The 3-factor Box Behnken Design and Response surface Quadratic models was used to optimize the formulations of liposomes and solid lipid nanoparticles respectively. The lipid nano-formulation showed good compatibility according to results of XRPD, FTIR and DSC. The PG-SLNs showed encapsulation efficiency of 84±0.5%, particle size of 103±46.04 nm with polydispersity index of 0.16±0.001 and zeta potential of -36±4.78 mV. The PG-liposomes showed 90 ± 3.6% encapsulation efficiency, 167.9 ± 3.5 nm average hydrodynamic diameter, 0.129 ± 0.002 PDI and -33.9 ± 4.5 zeta potential. *In vitro* drug release and permeation studies of both formulation in simulated nasal conditions were performed. Both lipid nanoformulations resulted in enhanced nasal permeability and sustained release of nanoformulation compared to the PG solution. The optimized formulations showed high potential to be used to target the brain via intranasal route.

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