

Enhanced oral delivery of Doxorubicin in a polysaccharide-lecithin core with solid lipid shell nanocarrier via transcellular pathway

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The present study reports an extensive evaluation of *in vitro* and *in vivo* enhanced oral delivery efficiency of newly-designed nanocarrier, with a solid lipid shell coating on polysaccharide-lecithin reverse micelles. This formulation (termed DSLNs) was loaded a model drug, doxorubicin (DOX) which is a substrate of p-glycoprotein, within the reverse micelles. As the results, intracellular concentration of doxorubicin in Caco-2 cells treated with free DOX was inhibited significantly with an increased concentration, as compared to that treated with DSLNs. In addition, a significantly improved permeability of DSLNs transporting across Caco-2 cell monolayers was demonstrated for eight-fold higher than that of free DOX. Permeability was inhibited at 4 °C and by endocytotic inhibitors pre-treated. Moreover, no apparent drop of TEER value indicated tight junction between Caco-2 cells was nearly intact during DSLNs treatment and therefore DSLNs likely transported across Caco-2 cell monolayers via transcytosis pathway. *In vivo* pharmacokinetic study, DSLNs demonstrated superior performance as evident by enhanced oral relative bioavailability up to 858.4% and prolonged circulation time to 72 h. This newly-designed lipid nanoparticle encourages a great potential to improve oral bioavailability of chemotherapeutic drug and *in vivo* therapeutic efficiency is examined in progress.

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