NOVEL NANOEMULSIONS FOR IMPROVED ORAL DELIVERY OF HYDROPHOBIC DRUGS

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Statement of Purpose: In order to enhance oral bioavailability of hydrophobic drugs, we have developed a series of nanoemulsion formulations. Paclitaxel was selected as a model hydrophobic drug whose oral bioavailability is significantly limited by P-glycoprotein expression in the small intestine.

Methods: The oil-in-water (o/w) nanoemulsions were made with pine nut oil as the internal oil phase, egg lecithin as the primary emulsifier, and water as the external phase. Stearylamine and deoxycholic acid were used to impart positive and negative charge to the emulsions, respectively**.** Nanoemulsions were prepared by sonication method and characterized for particle size, surface charge, and surface morphology. Tritiated [^{3}H]-paclitaxel in aqueous solution or when incorporated in the nanoemulsion formulations was administered orally to C57BL/6 mice and the biological distribution of the drug was examined. Non-compartmental pharmacokinetic analysis was performed to evaluate the relative enhancement in bioavailability of paclitaxel in the nanoemulsion formulations.

Results / Discussion: The formulated nanoemulsions had a particle size range of 25-200 nm. The nanoemulsions formulated with stearylamine and deoxycholic acid had a zeta potential of ~ +34 mV and ~ -45 mV, respectively. Following oral administration, a significantly higher concentration of paclitaxel was observed in the systemic circulation when administered in the nanoemulsion relative to control aqueous solution (Fig. 1). The absorbed drug was found to be predominantly distributed in the liver, kidneys, and lungs. Higher paclitaxel accumulation in the liver was observed from the nanoemulsion formulations as compared to the drug in aqueous solution form. Among the nanoemulsion formulations, those formulated with deoxycholic acid as a co-surfactant were most potent in enhancing the oral bioavailability of paclitaxel. We speculate that these formulations were able to transport drug through the bile acid transporter system.

Conclusions: Formulations of nanoemulsions were shown to generate enhancement in the oral bioavailability of paclitaxel, a model hydrophobic drug, relative to administration in aqueous solution. The results of this study suggest that nanoemulsions are promising novel formulations that can enhance the oral bioavailability of hydrophobic drugs.

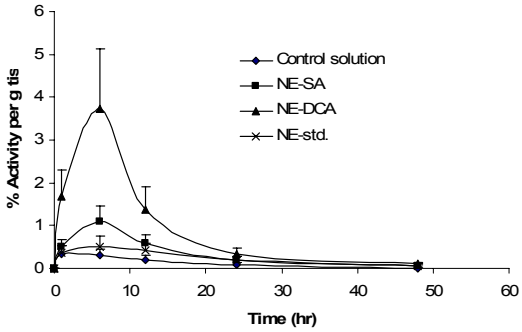

Figure 1. Plasma concentrations as a function of time following oral administration of ^{3}H-paclitaxel in the control and nanoemulsion formulations. SA and DCA are sterylamine and deoxycholic acid-containing nanoemulsions, respectively.

References:

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