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In Vitro Permeation and Pharmacokinetic Evaluations of a Novel Transdermal Formulation of CZ48, Lactone-Stabilized Camptothecin-C20-Propionate, for Cancer Treatment

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Camptothecin (CPT) is a promising anti-cancer agent with high efficacy against a variety of solid tumors. The lactone ring of CPT is essential for the anti-tumor activity but is unstable in vivo. A pro-drug of CPT, CZ48, has been developed where CZ48 is enzymatically hydrolyzed in vivo to active CPT. For its anti-cancer activity, CPT levels need to be sustained and maintained over a period of time, which means the requirement for a continuous delivery of CZ48. It has been demonstrated that I.V. bolus injection of CZ48 provided higher concentrations of the active CPT compared to direct dosing of CPT at the same dosing level in Sprague-Dawley rats. Also, it was shown that CZ48 dosing resulted in sustained plasma levels of CPT for five hours in this animal model. Therefore, if we extrapolate these observations to man, we would expect to see this pattern of sustained CPT levels upon administration of the pro-drug, CZ48. This means delivery of CZ48 can achieve a continuous, therapeutically relevant drug concentration of CPT for anti-neoplastic indications. Transdermal delivery satisfies the requirement for continuous CZ48 delivery since it allows for predictable and controlled drug permeation through the skin.A promising approach to deliver drug molecules transdermally is through a microemulsion formulation.Ourin vitro permeation data through excised rat skin as well asin vivo data upon topical application in Swiss-nude micedemonstrate the feasibility of achieving sustained plasma levels of CPT, required for anti-tumor activity, upon transdermal application of the pro-drug, CZ48.

Biography:

Dr. Rojeab is currently an Associate Professor of Pharmaceutics at the Raabe College of Pharmacy, Ohio Northern University inAda, OH, USA. He received his B.Sc. in Pharmacy in 1999 and Ph.D. in 2007 in Pharmaceutics from University of Houston, TX. He is also a licensed pharmacists in the states of OH, MI & TX. Current research in Dr. Rojeab's lab involves two main areas. First is the physicochemical characterization, preformulation, formulation and delivery of anti-cancer agents. The second research area involves bioavailability/bioequivalence evaluations of novel and conventional orally administered solid dosage forms in man.