

## Predicting the *In Vivo* Transdermal Iontophoretic Delivery of Luteinizing Hormone Releasing Hormone (LHRH) Using the Isolated Perfused Porcine Skin Flap

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### ABSTRACT

Peptides and proteins serve as hormones, enzymes, antigens, antibodies and structural elements in the body. In addition, they are involved in metabolic processes, immune defense mechanisms, cell growth and other biologic activities. With the advent of genetic engineering and other biotechnological techniques, economically feasible commercial production has made certain peptides and proteins available for treating many medical conditions. Peptide drugs are not orally active due to proteolytic enzymes in the gastrointestinal tract and extensive first-pass hepatic metabolism. Transdermal delivery of bioactive proteins and peptides has been suggested as a viable alternative route of administration. The large molecular size and charged character of peptides make them poor candidates for passive transdermal delivery. Transdermal iontophoresis is a novel technique for achieving percutaneous absorption of drugs. Using an applied electromotive force, drugs can be forced into the skin to be absorbed by the systemic circulation. The present study investigates the transdermal iontophoretic delivery of luteinizing hormone releasing hormone (LHRH), a peptide hormone, in an *in vitro* model system, the isolated perfused porcine skin flap (IPPSF), as well as *in vivo*. The study demonstrates for the first time the IPPSF's ability to predict *in vivo* serum concentrations of an iontophoretically delivered peptide. Using the flap's output profile as systemic input (much as one would use an IV infusion pump), and by taking into account system pharmacokinetics, which were best described by a two-compartment open model, the serum concentration-time profile can be accurately predicted. By separating out each contribution to variability, one can better assess the importance that both an individual animal's cutaneous absorption profile and systemic pharmacokinetics will have on iontophoretic delivery. It is also shown that the iontophoretically delivered hormone retains both its immunologic and biologic activity. (Supported by Becton Dickinson Research Centre, Research Triangle Park, NC)