Dermal Clearance, Elimination Half-life, and Apparent Volume of Distribution of Lidocaine And Prilocaine Are Independent of the Dose Delivered Directly in Dermis Using a Dermal Infusion Technique

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BACKGROUND

The purpose of this study is to investigate the dermal disposition of lidocaine (LDC) and prilocaine (PLC) when they are administered directly to the dermis via dermal microdialysis (dMD) probes, using a dermal infusion (DI) approach. [1] The results of these studies provide insights into whether cutaneous pharmacokinetics (cPK) is linear over a therapeutically relevant range and can be used to characterize the absorption kinetics (and possible interactions) of LDC and PLC from topically applied drug products when translated in clinical studies.

METHODS

Fifteen dMD probes were inserted on the shaved dorsum of four New Zealand albino rabbits and perfused with solutions of LDC, PLC, or both, across a range of concentrations (50 -500 µg/mL) for 6 hours, followed by saline for 5 hours (elimination phase). Two additional probes were perfused with normal saline only, to assess systemic redistribution of LDC and PLC. The dermal disposition parameters of clearance (dCl), apparent volume of distribution (dV_D), and elimination half-life ($dt_{1/2}$) were calculated, and then used to deconvolute the dermal concentrations at steady state to obtained the delivered dose to the dermis. [1]

The dermal infusion approach demonstrates that the dermal disposition of lidocaine and prilocaine is independent of the dose delivered directly to the dermis over a range of therapeutically relevant concentrations.

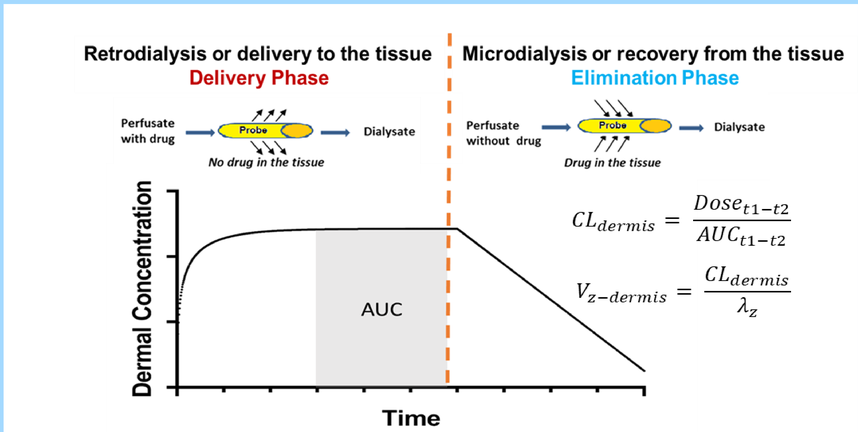

Figure 1. Dermal infusion technique consisting of retrodialysis and microdialysis

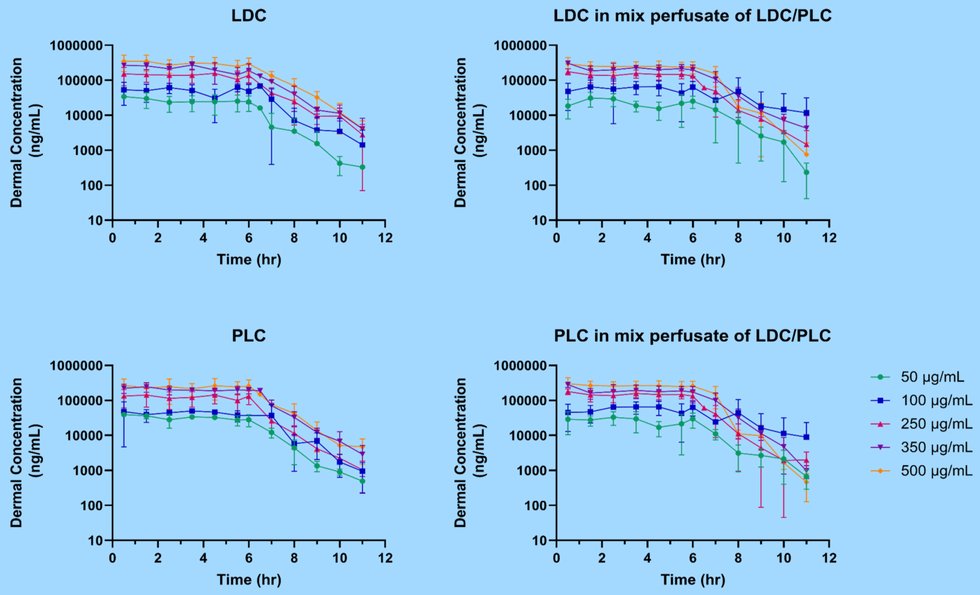

Figure 2. Average dermal concentration vs. time profiles of lidocaine (LDC) and prilocaine (PLC), alone or in mix perfusates following dermal infusion of LDC and PLC to 4 rabbits, 3 probes per concentration (mean ± SD, n=4)

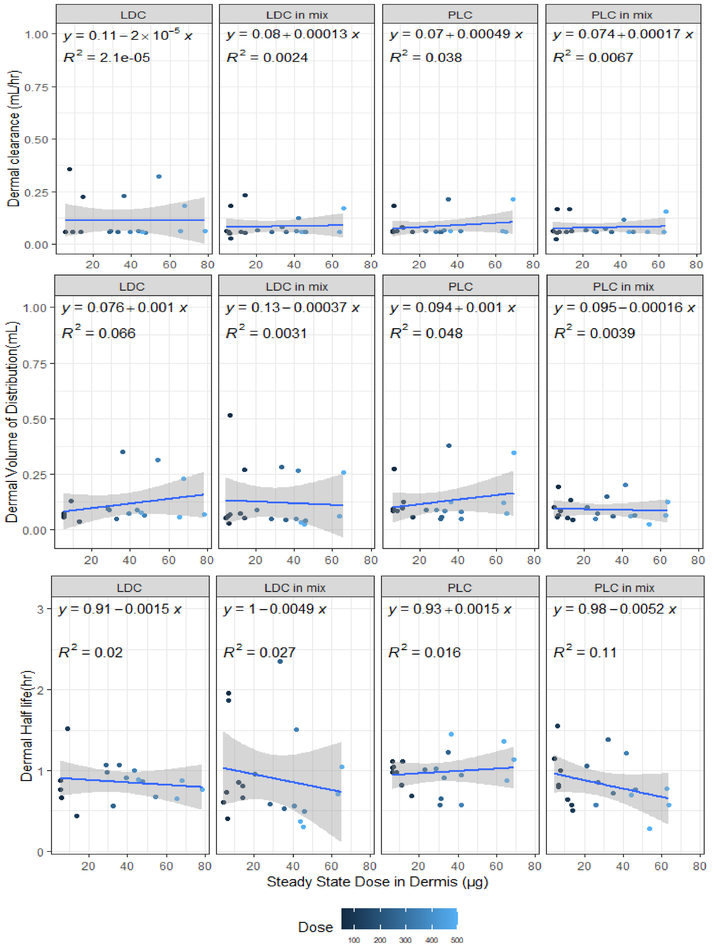

***Figure 3. LDC and PLC dermal clearance, volume of distribution, and half-life for different drug doses in the dermis at steady state, alone, or in presence of* another drug (data plotted for 5 different DI concentrations in 4 rabbits.**

RESULTS

There was a linear relationship between drug concentrations in dMD samples and the dose delivered via DI. Dermal disposition parameters were independent of the dose delivered within the tested range. When administered together, LDC and PLC did not appear to alter each other's dermal disposition parameters. Systemic redistribution to skin was negligible.

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REFERENCES

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