MPA in solution exhibited a steady state flux (3.8 ± 0.1 μg/cm^2/h) and permeability (1.1 × 10(−7) ± 3.2 × 10(−9) cm/s). MPA in Lipoderm exhibited a steady state flux of 1.12 ± 0.24 μg/cm^2/h, and permeability of 6.2 × 10(−09) ± 1.3 × 10(−9) cm/s across the biomimetic membrane. The cumulative release of MPA from Lipoderm, showed a linear single-phase profile with a R(2) of 0.969. In vivo studies with MPA in Lipoderm showed markedly higher local tissue MPA levels and lower systemic MPA exposure as compared to values obtained after intravenous delivery of the same dose of drug ($p < 0.05$). We successfully developed for the first time, a topical formulation of MPA in Lipoderm with optimal in vitro/in vivo permeability characteristics and no undesirable local or systemic adverse effects in vivo. Our study provides key preliminary groundwork for translational efficacy studies of topical MPA in preclinical large animal VCA models and for effectiveness evaluation in patients receiving VCA.

Fiala, S. et al. (2010). "A fundamental investigation into the effects of eutectic formation on transmembrane transport." *Int J Pharm* 393(1–2):68–73.

Eutectic systems enhance the permeation of therapeutic agents across biological barriers, but the mechanism by which this occurs has not previously been elucidated. Using human skin, it has proven difficult to isolate the fundamental effects of eutectic formation on molecule diffusion and partition from those that arise as a consequence of the simultaneous application of two agents. The aim of this work was to employ a model hydrophobic membrane to understand the fundamental permeation characteristics of two agents when applied as a eutectic mixture. Lidocaine and prilocaine were selected as model agents and infinite-dose permeation studies were carried out using precalibrated Franz diffusion cells with two thicknesses of silicone membrane. Membrane solubility was determined by HCl solution extraction and the membrane diffusion coefficients were calculated from the permeation lag times. The maximum permeation enhancement was achieved using a eutectic mixture at a 0.7:0.3 prilocaine/lidocaine ratio. A higher solubility of both agents in silicone membrane, enhanced diffusivity of prilocaine and superior release of both drugs, all contributed to produce enhanced permeation from the eutectic mixtures. Deconvolution of the transmembrane transport process suggests that the eutectic enhancement phenomena is a consequence of more favorable permeation characteristics of the two molecules in the absence of a formulation vehicle which competes in the transport process.

Folzer, E. et al. (2014). "Comparison of skin permeability for three diclofenac topical formulations: An in vitro study." *Pharmazie* 69(1):27–31.

Diclofenac is a hydrophilic nonsteroidal anti-inflammatory drug (NSAID) widely used in humans and animals. There are limited published studies evaluating diclofenac's skin permeation following topical administration. The aim of our study was to evaluate and compare the in vitro permeation of three different diclofenac-containing formulations (patch, gel, solution) over 24 hours. These formulations were applied ($n = 6$ per formulation) to pig skin sandwiched between the two chambers in a static Franz diffusion cell and aliquots from the receptor medium were sampled at predefined time points. An HPLC method with UV detection was developed and validated with the aim of characterizing the transepidermal penetration in the in vitro system. Using this assay to determine the permeation parameters, results at 24 hours showed that the Flector patch released the highest drug amount (54.6%), whereas a