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## Human skin permeation of Delta8-tetrahydrocannabinol, cannabidiol and cannabinol

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### Abstract

The purpose of this study was to quantify the in-vitro human skin transdermal flux of Delta8-tetrahydrocannabinol (Delta8-THC), cannabidiol (CBD) and cannabinol (CBN). These cannabinoids are of interest because they are likely candidates for transdermal combination therapy. Differential thermal analysis and in-vitro diffusion studies with human tissue were completed for the compounds. Heats of fusion, melting points and relative thermodynamic activities were determined for the crystalline compounds, CBD and CBN. Flux, permeability, tissue concentration and lag times were measured in the diffusion experiments. CBN had a lower heat of fusion and corresponding higher calculated relative thermodynamic activity than CBD. Ethanol concentrations of 30 to 33% significantly increased the transdermal flux of Delta8-THC and CBD. Tissue concentrations of Delta8-THC were significantly higher than for CBN. Lag times for CBD were significantly smaller than for CBN. The permeabilities of CBD and CBN were 10-fold higher than for Delta8-THC. Combinations of these cannabinoids with ethanol will be further studied in transdermal patch formulations in vitro and in vivo, as significant flux levels of all the drugs were obtained. CBD, the most polar of the three drugs, and other more polar cannabinoids will also be the focus of future drug design studies for improved transdermal delivery rates.

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