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# Investigation of iminosulfuranes as novel transdermal penetration enhancers: enhancement activity and cytotoxicity.

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## Abstract

**PURPOSE:** Very few chemical enhancers for transdermal drug delivery have been approved for clinical use due to irritancy and toxicity concerns. Novel chemical enhancers (iminosulfuranes) were synthesized and studied for their activity and toxicity.

**METHODS:** Skin was treated with 0.4 M 1-5 for 1 h before hydrocortisone was applied. Samples were taken over 24 h and analyzed by high-performance liquid chromatography. Dermal fibroblasts and epidermal keratinocytes were treated with 0-1.2 M 1-5 for 24 h and cytotoxicity assay [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT)] was performed. Furthermore, enhancement activity of 0-0.4 M 2 was studied. Partition coefficient of the model drugs into stratum corneum (SC) was measured and confocal Raman microscopy was used to study the penetration process and possible mechanisms of action of the enhancers. Quantitative structure-activity relationship (QSAR) was analyzed to study the contribution of different intramolecular descriptors to enhancement activity.

**RESULTS:** Iminosulfurane 2 showed the highest enhancement activity. All compounds below 0.2 M were safe to skin cells, and 2 was effective at the concentration of 0.1 and 0.2 M. Mechanisms of action of 2 may include increasing partition coefficient of the model drug into SC and interaction between the enhancer and lipids and protein in the SC. QSAR study indicated contribution of several factors to activity: partition coefficient, hydrogen-bond acceptor, and optimal molecular size.

**CONCLUSIONS:** Enhancement activity of 2 was achieved without any cytotoxicity.

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