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Effect of electric field on the enhanced skin permeation of drugs by electroporation

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Electroporation (voltage; 200 V) was applied using an exponentially decaying electric pulse generator on hairless rat skin using different shapes of electrodes, and the in vitro skin permeation of benzoate was measured as an index of the effectiveness of electroporation. Despite the same voltage of application, the skin permeation of benzoate was markedly different by the electrode shapes. Several experiments hereafter suggest that this reason was probably due to different 2-dimensional electric fields in the skin barrier, stratum corneum, and the voltage decreasing pattern applied. To confirm whether this phenomenon was specific for benzoate, diclofenac having a similar pKa was selected to carry out the same kind of examination. As a result, the skin permeability of diclofenac was influenced by 2-dimensional electric fields in the stratum corneum and the voltage decreasing pattern, similar to the benzoate permeation. Next, a rectangular pulse generator, where no decaying pattern was obtained for the application voltage, was used to measure the effect of electroporation on the skin permeation of diclofenac. As expected, the enhanced skin permeation of diclofenac was dependent only on the electric field when using the rectangular pulse generator. These results suggest that the electric field and time profile of the voltage (or AUC of voltage against time) at electroporation are very important factors to increase the efficacy of electroporation, and that the efficacy can be optimized by the shape of electrodes in addition to the application conditions of electroporation.