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The synergic effects of various electrolytes and electroporation on the in vitro skin permeation of calcein

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Various electrolytes in test solutions applied to the skin were evaluated with regard to their effects on enhanced skin permeation of calcein as a model permeant by electroporation (EP), which is a physical means to increase skin penetration by applying a high voltage pulse on the skin surface. Calcein solution (1.0 mM) containing different electrolytes at a concentration of 150 mM was applied to excised hairless rat skin, and a 10-ms electric pulse of 300 V was applied to the skin surface ten times (one pulse every second) at the beginning of the in vitro permeation experiments. The following results were obtained: (i) addition of several electrolytes, such as CaCl_2 and NaCl , further increased the EP-enhanced skin permeation of calcein when compared to treatment without these electrolytes; (ii) Ca^{2+} and Mg^{2+} exerted a greater effect than other cations (Na^+ , Zn^{2+} , Cu^{2+} , Fe^{3+} and Al^{3+}); (iii) with simultaneous application of CaCl_2 and EP, the effect of anodal EP was much greater than that of cathodal EP; (iv) the penetration-enhancing effects of CaCl_2 were also obtained with EP pretreatment followed by calcein addition; and (v) skin permeation was greatly increased particularly with simultaneous application of EP and Ca^{2+} . These substantial combined synergic effects of EP and electrolytes, particularly those containing CaCl_2 , MgCl_2 and CaBr_2 , may be related to the disruptive and retrievable functions of the biggest barrier of skin, the stratum corneum, of these electrolytes.