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The Enhancing Effect of a Triethanolamine-Ethanol-Isopropyl Myristate Mixed System on the Skin Permeation of Acidic Drugs

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The effect of a TEI enhancer mixed system consisiting of triethanolamine (T), ethanol (E) and isopropyl myristate (IPM) on the skin permeation of acidic, basic and neutral drugs were evaluated *in vitro* using excised hairless rat skin. The binary enhancer system consisting of IPM and ethanol (EI) produced marked improvement on the penetration of all the drugs tested. When T was added to the EI system, a greater enhancing effect was found only on acidic drugs with a carboxyl group, compared with the flux in the EI system. On addition of another amine to the EI system, instead of T, mefenamic acid (MA), which exhibited the highest enhancing effect of the model drugs, showed an approximately 14-180 times greater flux than when delivered by the EI system. On simultaneous application of isosorbide dinitrate (ISDN) with MA in the TEI system, the flux of MA increased on increasing the T concentration in the TEI system, while, the flux of ISDN, a neutral drug, was unaffected by the T concentration. Application of MA in the EI system after pretreatment of the TEI system showed that the residual amount of T in the skin plays an important role in the skin permeation of MA. Furthermore, at a fixed concentration of MA, the flux of MA increased on increasing the T concentration in the TEI system, while the flux of E remained unchanged. Finally, the infrared spectrum of MA with amine in the E solution indicated that the carboxyl group of MA was ionized. These results demonstrated that the formation of an ion pair between MA and T, but not the effect of T on the skin, may be responsible for the enhanced skin permeation of MA using the TEI system.