

〈原 著〉

## 動物実験代替法として三次元培養皮膚モデルを用いた *In vitro* 経皮吸収試験に関する研究

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### Studies for *In Vitro* Percutaneous Absorption Using Three-Dimensional Skin Tissues in Alternative Animal Experiments

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#### Abstract

Recently it becomes easy to purchase the three-dimensional skin tissues in Japan whose solidity and quality are improving speedily. Regarding to the alternatives to animal experiences, the application of several compounds to the percutaneous permeation was examined by using the three-dimensional skin tissues. Sodium benzoate (BA), resorcin (RN), salicylic acid (SA), methylparaben (MP), ethylparaben (EP) and 4-chloro-m-cresol (CC) were selected as the test compounds and TESTSKIN LSE-High and Vitrolife-Dermis were used as the three-dimensional skin tissues. The flux obtained from SA was the lowest on comparison with the fluxes obtained from the other 5 compounds. The fluxes of 5 permeants except SA obtained from TESTSKIN LSE-High were 2.6 to 11.4 times higher than those from the abdominal skin of guinea-pig and then those from Vitrolife-Dermis were 2.5 to 7.7 times higher than those from the abdominal skin of guinea-pig. Relationship between  $\log k'$  ( $k'$ : capacity factor by HPLC) and the fluxes of 4 permeants having the phenolic function except SA obtained from the abdominal skin of guinea-pig was in good agreement ( $p < 0.01$ ). But there were no relationships between  $\log k'$  and the fluxes obtained from either TESTSKIN LSE-High or Vitrolife-Dermis. On the contrary the fluxes of 5 permeants except SA obtained from TESTSKIN LSE-High had the correlation ( $p < 0.05$ ) with those obtained from Vitrolife-Dermis. On treating TESTSKIN LSE-High with 10 mM sodium dodecylsulfate (SDS) for 30 min, the fluxes of BA, RN, and SA became 0.6, 0.2, and 0.5 times lower, respectively. In the case of the treatment of TESTSKIN LSE-High with 10 mM benzalkonium chloride (BK), the fluxes of BA and SA showed the low value to 0.4 times and the high value to 3.4 times, respectively. On the other hand, the treatment of Vitrolife-Dermis with 10 mM-BK made the flux of MP and EP to increase to 1.4 times and the flux of SA to lower to 0.7 times.

**Key words:** three-dimensional skin tissues, percutaneous absorption, preservatives, flux, abdominal skin of guinea-pig.