Title of Research:
21-3-01
Establishment of in silico model to predict skin absorption of chemical compounds with two-layered diffusion model

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Summary of Research:
Purpose: The skin is exposed to many chemical substances, including pharmaceuticals, cosmetics, and fragrances, and is inadvertently exposed to many chemical substances in daily life. Therefore, it is extremely important to evaluate the skin permeability of chemical substances that may contact the skin. Next-generation risk assessment (NGRA), a risk assessment method that combines various methods without using animals, has attracted much attention in recent years. In the present study, development of in silico model that predict dermal absorption after chemical exposure under real-world condition, finite dose, was investigated by considering changes in concentration of the applied substance on the skin surface.
Methods: Prediction of skin permeation parameters: Physicochemical parameters of various chemical substances were calculated using Scigress software. Diffusion and distribution coefficients, which are skin permeation parameters of chemicals, were predicted by random forest regression analysis, an ensemble learning algorithm, using the statistical software JMP Pro16 with physicochemical parameters as descriptors.
Results and conclusion: The study using random forest regression analysis showed that all of the skin permeation parameters were well predicted when regression analysis was performed using M.W., ClogP, HOMO, and LUMO as descriptors. Skin permeation profiles, calculated by two-layer diffusion model after chemical exposure under finite dose condition, showed good perdition results when water volatilization rate constant was considered. There were, however, some deviations between the predicted and observed skin permeation profiles, the overall prediction results were good. These results suggest that the constructed model would be used to predict the dermal absorption of finite dose systems.

Timeline:
March 1st, 2021-

Topics:
2022 ICCA-LRI & NITE Workshop（June 20, 2022）
 In silico estimation of skin permeation of chemicals with their diffusion and partition parameters
2022 年 LRI Annual Workshop（August 26, 2022）
 Establishment of in silico model to predict skin absorption of chemical compounds with two-layered diffusion model