THE SELECTED ABSTRACTS

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236 Significance of octanol-water partition coefficient and molecular weight as molecular descriptors in predicting skin permeability of chemical substances

Y.C. Chang[1], Chen[1], Chen[2]
[1]China Medical University, Taichung, Taiwan
[2]National Kaohsiung First University of Science and Technology, Kaohsiung City, Taiwan

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Abstract
Objectives: The occupational hazard of chemical absorption via dermal route was frequently assessed by evaluating the skin permeability (Kp) of chemical. In addition to *in vitro* testing using human skin, the quantitative structure-activity relationship (QSAR) has been employed as an alternative source to providing Kp. In the early Kp QSARs the octanol-water partition coefficient (log K_{OW}) and molecular weight (MW) were commonly applied as dominant properties to describe transdermal transport of chemical. This study examined the efficacy of log K_{OW}-/MW-based QSARs in Kp prediction.
Methods: One hundred and fifty-eight chemicals of known Kp determined *in vitro* using human skin were used to evaluate the goodness of fit (R^2) of the model estimates approximating the measured Kp for six log K_{OW}-/MW-based Kp QSARs reported in Wilschut et al. (1995) and Mitragotri (2002). A new Kp QSAR consisting of additional descriptors for the same compounds was developed by identification of key descriptors from a pool of 3,224 descriptors supported by Dragon® followed by stepwise regression.
Results: For the log K_{OW}-/MW-based Kp QSARs, the regression of model estimates against experimentally determined Kp yielded R^2 of 0.314 to 0.744, with the lowest value observed for the model employing log K_{OW} alone. In the new QSAR, in addition to log K_{OW} the electrostatic distribution in the molecular space appeared to be a significant factor affecting Kp, while the MW exerted its influence as a sub-domain, thus under constraints, of antineoplastic properties.
Conclusions: As the Kp QSAR continues to evolve, attention may be required of on interpreting the limitations of MW as a Kp descriptor. Four of the investigated Kp QSARs show a R^2 close to 0.7 or higher when predicting Kp, suggesting a consistent performance of these models to serve as a tool of dermal hazard characterization.

Abstract

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Author	Chang, Yen-Ching, China Medical University, Taichung, Taiwan (Presenting author)
Co-author(s)	Chen, Chen-Peng, China Medical University, Taichung, Taiwan Chen, Chan-Cheng, National Kaohsiung First University of Science and Technology, Kaohsiung City, Taiwan
Topic	Hazard identification

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