Prediction of Toxicity of Phenols and Anilines to Algae by Quantitative Structure-activity Relationship[1]

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Objective To measure the toxicity of phenol, aniline, and their derivatives to algae and to assess, model, and predict the toxicity using quantitative structure-activity relationship (QSAR) method. **Methods** Oxygen production was used as the response endpoint for assessing the toxic effects of chemicals on algal photosynthesis. The energy of the lowest unoccupied molecular orbital (E_{LUMO}) and the energy of the highest occupied molecular orbital (E_{HOMO}) were obtained from the ChemOffice 2004 program using the quantum chemical method MOPAC, and the frontier orbital energy gap (ΔE) was obtained. **Results** The compounds exhibited a reasonably wide range of algal toxicity. The most toxic compound was α-naphthol, whereas the least toxic one was aniline. A two-descriptor model was derived from the algal toxicity and structural parameters: $\log 1/EC_{50}=0.268\log K_{ow}-1.006\Delta E+11.769$ (n=20, r^2=0.946). This model was stable and satisfactory for predicting toxicity. **Conclusion** Phenol, aniline, and their derivatives are polar narcotics. Their toxicity is greater than estimated by hydrophobicity only, and addition of the frontier orbital energy gap ΔE can significantly improve the prediction of $\log K_{ow}$-dependent models.

Key words: Toxicity; QSARs; Frontier orbital energy gap; Prediction

REFERENCES

1. Könemann H, Musch A (1981). Quantitative structure-activity relationships in fish toxicity studies. Part 2: the influence of pH on the QSAR of chlorophenols. *Toxicology* **19**, 223-228.
2. Cronin M T D, Schultz T W (1996). Structure-toxicity relationships for phenols to *Tetrahymena pyriformis*. *Chemosphere* **32**, 1453-1468.
3. Lu G H, Yuan X, Wang C (2003). Quantitative structure-toxicity relationships for substituted aromatic compounds to *Vibrio fischeri*. *Bull Environ Contam Toxicol* **70**, 832-838.
4. Lin J H, Kao W C, Tsai K P, *et al*. (2005). A novel algal toxicity testing technique for assessing the toxicity of both metallic and organic toxicants. *Water Res* **39**, 1869-1877.
5. Lu G H, Yuan X, Zhao Y H (2001). QSAR study on the toxicity of substituted benzenes on the algae (*Scenedesmus obliquus*). *Chemosphere* **44**, 437-440.
6. Du C J, Chu D S (1994). Water Quality Analysis Base in Environmental Monitoring. Harbin, P. R. China: Science and Technology Press of Heilongjiang.
7. Bradbury S P (1994). Predicting modes of toxic action from chemical structure: an overview. *SAR QSAR Environ Res* **2**, 89-104.
8. Kamlet M J, Doherty R M, Taft R W, *et al*. (1986). Solubility properties in polymers and biological media. 7. An analysis of toxicant properties that influence inhibition of bioluminescence in *Photobacterium phosphoreum* (the Microtox Test). *Environ Sci Technol* **20**, 690-695.
9. Mielczarek C (2005). Acid-base properties of selected flavonoid glycosides. *Eur J Pharmac Sci* **25**, 273-279.
10. Yan X F, Xiao H M, Gong X D, *et al*. (2006). A comparison of semiempirical and first principle methods for establishing toxicological QSARs of nitroaromatics. *J Mol Struct: Theochem* **764**, 141-148.

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