以密閉式藻類毒性試驗方法評估有機物之毒性與結構-活性關係之研究

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摘　要

此篇研究歸納本實驗室以月芽藻 (*Pseudokirchneriella subcapitata*)所進行之 48 小時密閉式毒性試驗所得到的結果，利用藻細胞的數量變化(Final yield)做為觀測終點，藉由Probit模式求出半致死濃度 (50% Effect concentration，EC_{50})，並將九十一種有機物的毒性機制分成五大類，共包含了Non polar narcosis、Polar narcosis、Oxidative phosphorylation uncoupling、Electrophilic/Proelectrophilic、和Respiratory inhibition。對於毒性機制屬於Non polar narcosis的有機物，將其毒性試驗後所得到的 $\log(1/EC_{50})$，與辛醇-水係數 (1-octanol/water partition coefficient，log P)進行回歸分析，找出基線毒性 (Baseline toxicity)方程式：

$\log(1/EC_{50}) = 0.739 \log P + 2.051$，n= 43，$R^2 = 0.860$。

本研究利用有機物的超額毒性 (Excess toxicity)，與上述所求得的基線毒性比較之後，可發現醛類、酚類和腈類的毒性皆高於基線毒性一個 order 以上。而從各種有機物的 log ACR 中，可發現月芽藻對酮類的毒性容忍範圍較小，對醛類的毒性容忍範圍較大。

本研究選用不同的物理和化學相關參數，包括log P、E_{lumo}、E_{homo}、EE、CCRe、dipole、R、πH、$\sum\alpha^{H}$、$\sum\beta^{H}$，針對上述的五種毒性機制，進行定量結構與活性關係 (Quantitative Structure-Activity Relationship, QSAR)之分析，討論有機物毒性與參數之間的相關性，進而找出最適合預測毒性的方程式。

最後，參考其他文獻中，以不同的生物體所進行毒性試驗的結果，與本研究結果比較，發現除了水蚤 (*Daphnia magna*)對於苯胺類的毒性較敏感之外，本實驗方法對於大部份的有機物和試驗物種，在毒性偵測上，均較其他實驗方法來得敏感；同時亦發現在不同的毒性機制下，本研究方法與其他物種的毒性試驗結果，有很高的相關性，尤其是毒性機制屬於 Non polar narcosis 的有機物，以 fathead minnow (*Pimephales promelas*)與本研究結果的相關性最高，可做為替代物種 (Surrogate)選擇的參考。

The Study of Toxicity Assessment of Organic Chemicals Using a Closed-System Algal Test and the Quantitative Structure-Activity Relationships

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Abstract

This research assayed the 50% effective inhibition concentration 48h-EC_{50} of 91 organic chemicals to the algae（*Pseudokirchneriella subcapitata*), by using 300-ml BOD closed bottle system. The inhibition rate was calculated from the changes of cell numbers, and the 48h-EC_{50} was determined by the Probit model. These 91 organic chemicals can be classified into 5 categories by their mechanism of toxic action, including Non polar narcosis, Polar narcosis, Oxidative phosphorylation uncoupling, Electrophilic/Proelectrophilic, and Respiratory inhibition.

The baseline toxicity equation was based on the Non polar narcosis and was defined using hydrophobicity, as calculated log 1-octanol/water partition coefficient (log P): [$\log(1/EC_{50})= 0.739 \log P+ 2.051$, n= 43, $R^2= 0.860$]. The present study proposed excess toxicity (log Te)to compare the toxicity of other

chemicals with the baseline toxicity as mentioned above. The result showed that the log Te of aldehydes, phenols, and nitriles is more than 1 , that means their toxicity is more toxic than baseline toxicity in one order. Using the acute to chronic ratio (log ACR), it showed that the range of toxicity to ketones that the algae (*Pseudokirchneriella subcapitata*) can endure was the narrowest; on the other hand, the aldehydes was the broadest.

In order to develop quantitative structure-activity relationships (QSARs), this study used different physicochemical parameters including log P, E_{lumo} (Energy of the lowest unoccupied molecular orbital), E_{homo} (Energy of the highest occupied molecular orbital), EE (Electronic energy), CCRe (Core-core repulsion), dipole, R (Excess molar refraction), πH (Solute's dipolarity/dipolarizability), $\sum\alpha^{H}$ (Solute's effective or summation hydrogen-bond acidity), $\sum\beta^{H}$ (Solute's effective or summation hydrogen-bond basicity). Under different mechanism of toxic action, the discriminating parameters can be chosen to predict the toxicity effectively.

Finally, results from this study show the algae (*Pseudokirchneriella subcapitata*) are very sensitive to organic toxicants, except anilines. This study showed the water flea (*Daphnia magna*) was very sensitive to anilines when the log P of anilines was below 3. The correlation for Non polar narcosis between the results of this study and fathead minnow (*Pimephales promelas*) showed that these two species can be chosen as good surrogates.