The use of QSAR in ecotoxicity and the evaluation of the effect on the environmental organisms

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1. Introduction

Environmental risk or hazard assessment is based on a comparison of the concentration of a chemical in the environment and the concentration of a chemical at which no adverse effects on the environment are observed. The concentration in the environment after the released of a chemical can be measured or estimated with fate modeling techniques. Many test methods using environmental organisms have been proposed and established to determine no observable effect concentration(NOEC) and L(E)C50. But, the number of chemicals in the market are too many to carry out the tests for all of the chemicals. Quantitative structure-activity relationship(QSAR) is a help in assessing the chemical toxicity. Although this technique has been applied in drug design for many years, there are some differences in the application to ecotoxicity.

In order to assess the risk level of a chemical or in an area, the ratio of these two concentrations is used. Eco-toxicological risk quotient(ERQ) is an index which is proposed by the author for this purpose.

2. Quantitative Structure-Activity Relationship(QSAR)

QSAR needs three kinds of data;

1) biological toxicity

2) selection of chemicals and description of characteristics of the chemicals

3) statistical method to combine 1) and 2).

Any biological toxicity data(EC50,LC50,NOEC) can be use in QSAR. It is preferable that the data is obtained by an authorized test method, the same organisms is used in the test and the reliability of the data is confirmed by the specialist.

The selection of chemicals of the same mode of action is important to get an reliable relation. The parameters used in QSAR are the representatives of lipophilic, steric and electric characters of chemicals. Log(Pow; n-octanol/water partition) is a most used lipophilic parameter. Topological parameters are also used in describing the characteristics of chemical structure. In some cases, index value is used to distinguish the mode of action. There is no theological way to find beforehand whether a chemical acts in the same mode as the chemical group used to derive the regression formula or not. It will be decided by try and error and through experience. If various kinds of chemicals is employed without the hypothesis of the same mode of action, much attention should be paid for interpretation.

Polynomial regression analysis is mainly used as an statistical method, though discriminate analysis is employed in some cases.

Some examples of QSAR analysis will be discussed.

3. Eco-toxicological Risk Quotient(ERQ)

In order to evaluate the hazardousness, we propose Eco-toxicological Risk Quotient(ERQ) was defined as follows;

$$ERQ_c = -\log \frac{\text{Concentration in the environment}}{\text{Effective concentration in the test}}$$

$$ERQ_a = -\log \sum \frac{\text{Concentration in the environment}}{\text{Effective concentration in the test}}$$

ERQ_c and ERQ_a are the indices of the hazardousness of a chemical and chemicals in an area, respectively. ERQ_a is defined under the hypothesis that the chemical toxicity is additive and can be used for composite pollution. ERQs in water environment of Japan were calculated and could explain the status of water pollution. ERQ numerates the hazardousness and can be a help to find the chemical which should be kept under observation and to see whether the chemical pollution is improved or worsened. This idea is recently developed to ERQ in which maximum tolerance concentration (MTC) is used as the effective concentration in the test.