P005 Detection of mutagenic/carcinogenic nitroarenes in surface soil

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Organic extracts of surface soil samples collected at 5 sites, i.e. Kyoto, Takatsuji, Izumiotsu, Nagoya, and Hekinan, showed strong mutagenicity in S.typhimurium TA98 without S9 mix. To clarify mutagenic constituents in these 5 soil samples, organic extracts were separated by chromatography using a Sephadex LH-20 column and a silica gel column. Resulting fractions with potent mutagenicity were subsequently separated by low-pressure liquid chromatography (LPLC) using an Ultra pack ODS column, and the fractions with the highest mutagenicity were obtained at elution volumes of 48-84 ml for the 5 soil samples. These fractions were further separated by HPLC using COSMOSIL 5C18 AR-II, Luna 5 μ Phenyl-Hexyl, and Inertsil ODS-EP columns. Consequently, it was revealed that the mutagenic potency of these fractions was attributed to 1,6- and 1,8-dinitropyrene, 1,3,6- trinitropyrene, and 3,9-dinitrofluoranthene. 3,6-Dinitrobenez [ε]pyrene was also detected in the second-highest mutagenic fractions prepared from the 5 soil samples by LPLC described above. The sum of contribution ratios of these 5 nitroarenes to the mutagenicity of the each soil extract were from 54% to 70%.

変異・がん原性モノトロアーレーンの表層土壌中の検出
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P006 Discussion about a method for cancer risk evaluation of DDT and its metabolite

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The purpose of our study is to evaluate the cancer risk of chemical substances from in vitro testing results. We performed a transformation assay by organic chlorine insecticide, Dichlorodiphenyltrichloroethane (DDT), and its metabolite, Dichlorodiphenyldichloroethylene (DDE), on BALB/3T3 cells. From the transformation assay, we got the dose-response curve for DDE, of which the formula was P(tumor DDE)=1-exp{-(5.5x10⁻⁴D-7.1x10⁻⁴D²)} (R=0.99); then P(tumor DDE) was probability of transformation and D was AUC (g/L·hours), by applying a linear-quadratic model. We used the Area Under the Curve (AUC) for dose in this formula since transformation activity is dependent both on time and concentration. We also developed a PBPK (physiologically-based pharmacokinetics) model for DDT, which estimate the variation of concentration with the time in a certain tissue. As for DDT, liver is a target organ and the calculated AUC of DDT and DDE in the liver for the single dose of 1(mg/kg/day) was 0.0056 (mg/kg·hours) and 0.0012 (mg/kg·hours), respectively. The AUC values were applied in the DDT dose response curve to estimate the probability of transformation in a liver cell. The number of liver cells in human was estimated 7x10¹⁴ (cells), therefore the cancer risk of DDT was calculated as 0.1per (mg/kg/day), which was about one-third of the estimation by EPA.

代謝物の毒性を考慮したDDTの発がんリスク評価方法の検討
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