GENOTOXICITY OF HIGHLY TOXIC ORGANOCHLORINE CONGENERS IN CULTURED HUMAN LYMPHOCYTES

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OBJECTIVE

Our human bodies have already been contaminated with various chemicals including the highly toxic organochlorine compounds such as 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD), 2,3,4,7,8-pentachlorodibenzofuran (PeCDF) and 3,4,5,3',4'-pentachlorobiphenyl (PeCB). In this study, in order to evaluate the genotoxicity of these three chemicals, we examined their effects on the induction of both micronuclei (MNs) and sister chlomatid exchanges (SCEs), which have frequently been utilized as indicators of biological damage due to exposure to different carcinogens or mutagens , in cultured human lymphocytes.

APPROACH AND METHODS

Healthy Japanese have already been contaminated with very toxic organochlorine compounds such as polychlorinated dibenzofurans (PCDFs), polychlorinated dibenzo-p-dioxins (PCDDs) and coplanar polychlorinated biphenyls (Co-PCBs) and their total concentration in the Japanese is considered to be 60 to 80 ppt as TCDD toxic equivalent on fat weight basis. We assumed that the total concentration of the organochlorine compounds in the Japanese was 70 ppt as TCDD toxic equivalent in fat basis and that toxic equivalency factors (TEFs, relative to TCDD) were 0.5 for PeCDF and 0.2 for PeCB. Genotoxicity of TCDD, PeCDF and PeCB was investigated by using the induction of MNs and SCEs in cultured human lymphocytes at doses of about 5, 25 and 50 times higher concentration than 70 ppt in TCDD toxic equivalent. Therefore, human lymphocytes were treated with TCDD at final concentration of 364, 1,470 and 2,940 ppt, with PeCDF at 784, 3,948 and 7,896 ppt and with PeCB at 1,750, 8,750 and 17,500 ppt. Chemicals, experi-

mental procedures and statistical analysis were previously described in detail[1].

RESULTS

The effects of TCDD, PeCDF and PeCB on the induction of both MNs and SCEs with and without 7,8-benzoflavone (ANF) were examined, because the culture of human lymphocytes with ANF in vitro seemed to provide much more sensitive tool to detect exposure to carcinogens or mutagens[2,3,4]. ANF significantly enhanced the frequency of MNs and of SCEs ($P<0.01$). Regardless, however, of the presence or absence of ANF, TCDD, PeCDF and PeCB markedly increased the frequency of MNs and SCEs with almost the same dose-dependent manner. Dose-response relationships between the concentration of TCDD, PeCDF and PeCB and the frequency of MNs and SCEs without ANF are shown in Figs. 1 and 2, respectively. The 50% effective concentration (EC_{50}) of the induction of MNs and SCEs seemed to be around 10^3 times higher level than the average one of the Japanese, namely 70 ppt as TCDD toxic equivalent.

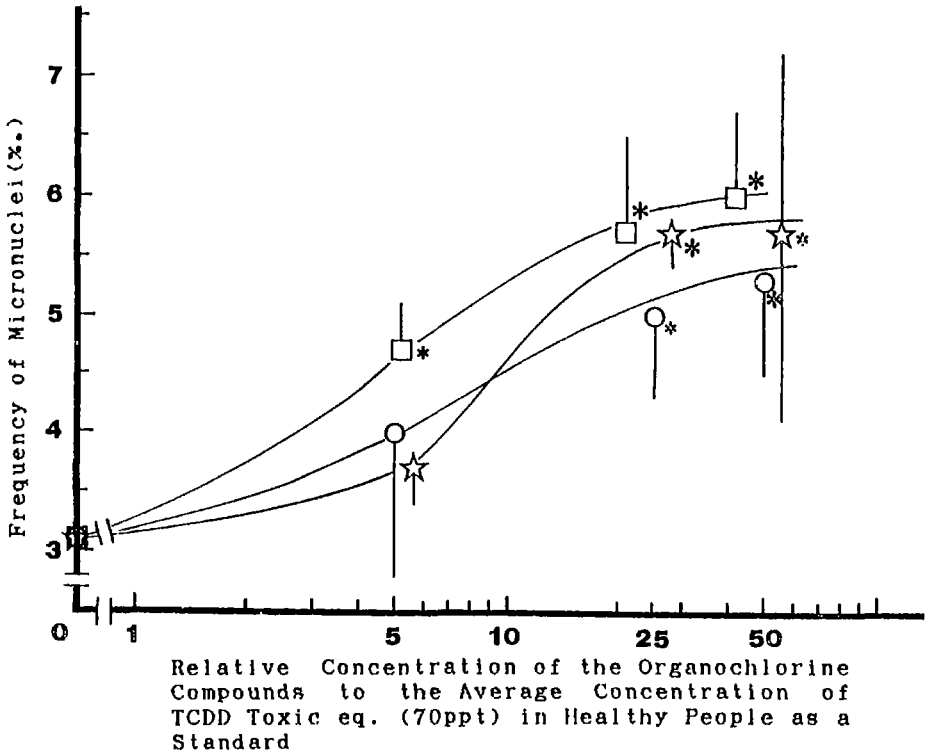

Fig.1. Effects of TCDD(□), PeCDF(☆) and PeCB(○) on the induction of micronuclei in human whole-blood cultures
* : $P<0.05$, * : $P<0.01$

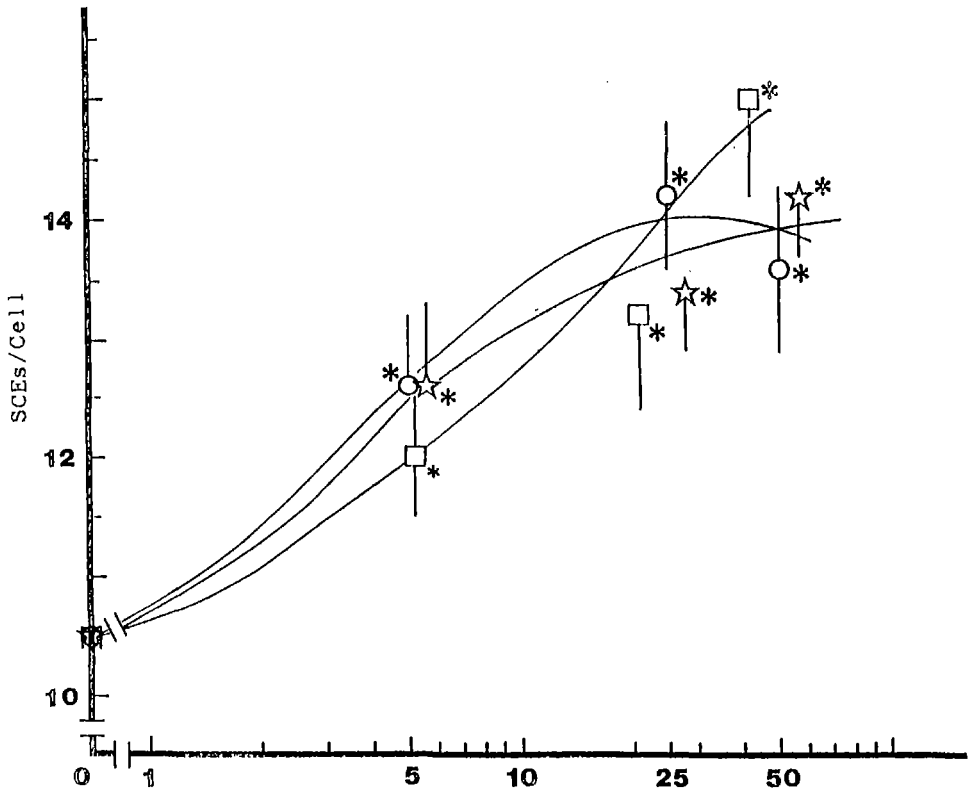

Fig.2. Effects of TCDD(□), PeCDF(☆) and PeCB(○) on the induction of SCEs in human whole-blood cultures
* : P<0.05, * : P<0.01

CONCLUSIONS

1) The respective TEF values of 0.5 and 0.2 for PeCDF and PeCB were considered to be reasonable so far as the induction of MNs and SCEs was employed as indicators of their genotoxic potency.
2) TCDD, PeCDF and PeCB were regarded as highly genotoxic chemicals because EC_{50} of the induction of both MNs and SCEs appeared to be only about 10 times higher concentration than the mean one of healthy Japanese people.
3) Accordingly, one of the most important problems which should be solved is further comprehensive genotoxicity and/or health consequences of the mixed contamination of these chemicals to the descendants.

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