EVALUATION OF GENOTOXIC EFFECTS OF ORGANOCHLORINE COMPOUNDS RETAINED IN HUMAN BODY USING IN VITRO TEST SYSTEMS

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OBJECTIVE

Our human bodies have already been contaminated with various chemicals including the highly toxic organochlorine compounds such as polychlorinated dibenzo-p-dioxins (PCDDs), polychlorinated dibenzofurans (PCDFs) and coplanar polychlorinated biphenyls (Co-PCBs). In this work, in order to evaluate their genotoxic effects in vitro, we prepared the mixture of PCDDs, PCDFs and Co-PCBs, which very resembled their contamination in healthy people in their composition, and investigated the effects of the mixture on the induction of both micronuclei and sister chromatid exchanges (SCEs), which have frequently been utilized as indicators of genetic damage due to exposure to different carcinogens or mutagens, in human whole-blood cultures.

APPROACH AND METHODS

Healthy Japanese people have already been contaminated with some highly toxic congeners of PCDDs, PCDFs and Co-PCBs and their total concentration in the Japanese is considered to be 60 to 80ppt as 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) toxic equivalent on fat weight basis. We assumed that the total concentration of these organochlorine compounds in the

Japanese was 70ppt as TCDD toxic equivalent.Genotoxic effects of the mixture of the organochlorine compounds were evaluated by using *in vitro* induction of micronuclei and SCEs of the lymphocytes in human whole-blood cultures at doses of 2 to 60 times higher concentration than 70ppt as TCDD with or without 8×10^{-5} M 7,8-benzoflavone (ANF), because the *in vitro* culture of human lymphocytes in the presence of ANF seemed to provide much more sensitive tool to detect exposure to carcinogens or mutagens[1,2,3]. Chemicals, experimental procedures and statistical analysis were previously described in detail[4].

RESULTS

Experimental results concerning the dose-response relationship between concentration of the mixture and the frequency of micronuclei and of SCEs are indicated in Figs 1 and 2. ANF markedly enhanced the frequency of SCEs at any dose levels of the mixture, particularly at higher doses and slightly increased the frequency of micronuclei at lower dose levels. Regardless, however, of the presence of ANF, the mixture of organochlorine compounds significantly elevated the frequency of both micronuclei and SCEs with fairly good dose-dependent manner. The 50% effective concentration (EC_{50}) of the induction of micronuclei and SCEs seemed to be 5 or 6 times higher level than the average concentration in the Japanese, namely 70ppt as TCDD.

CONCLUSIONS

1) The mixture of PCDDs, PCDFs and Co-PCBs, which resembled their contamination in healthy Japanese people in their composition, was regarded as highly genotoxic chemicals because EC_{50} values of the in vitro induction of micronuclei and SCEs appeared to be only about 5 times higher concentration than the mean one in healthy Japanese people, namely 70ppt as TCDD.
2) Accordingly, one of the most important problems which should be solved is further comprehensive genotoxic effects and/or health consequences due to the mixed contamination of these organochlorine compounds to the descendants.

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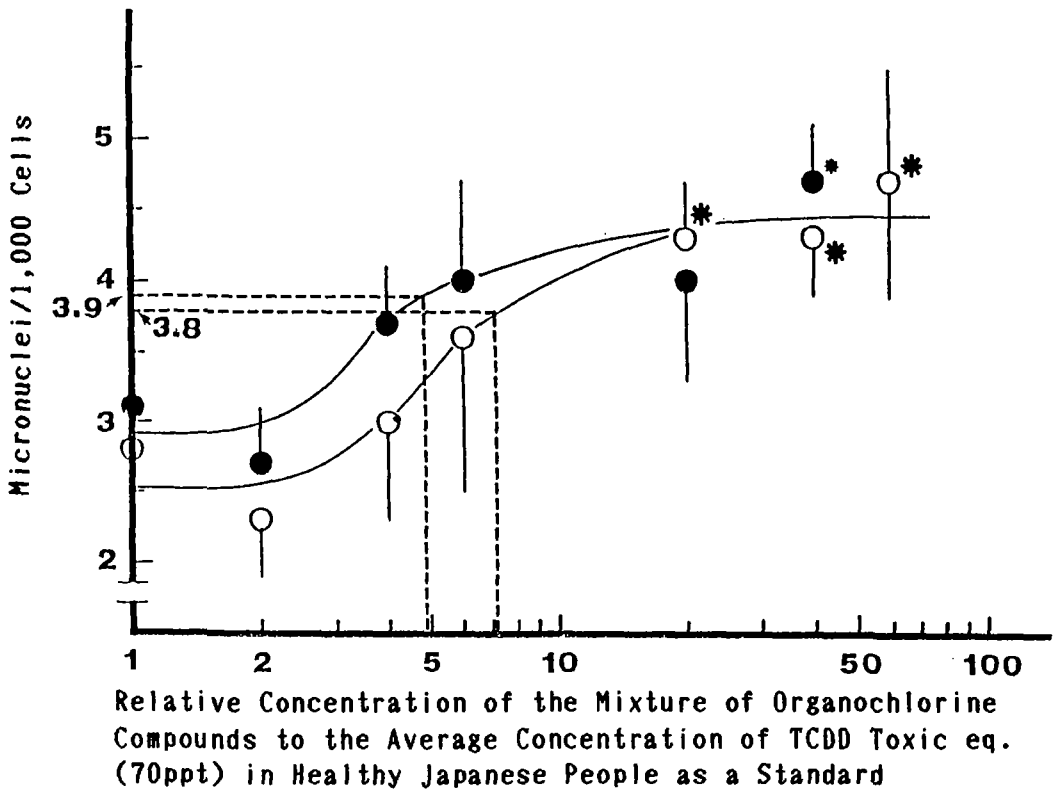

Fig.1. Effects of the mixture of PCDDs, PCDFs and Co-PCBs retained in healthy Japanese people on the induction of micronuclei
○ : Mixture of PCDDs, PCDFs and Co-PCBs only
● : Mixture of PCDDs, PCDFs and Co-PCBs plus ANF(8×10^{-5}M)
* : $P<0.05$, ** : $P<0.01$

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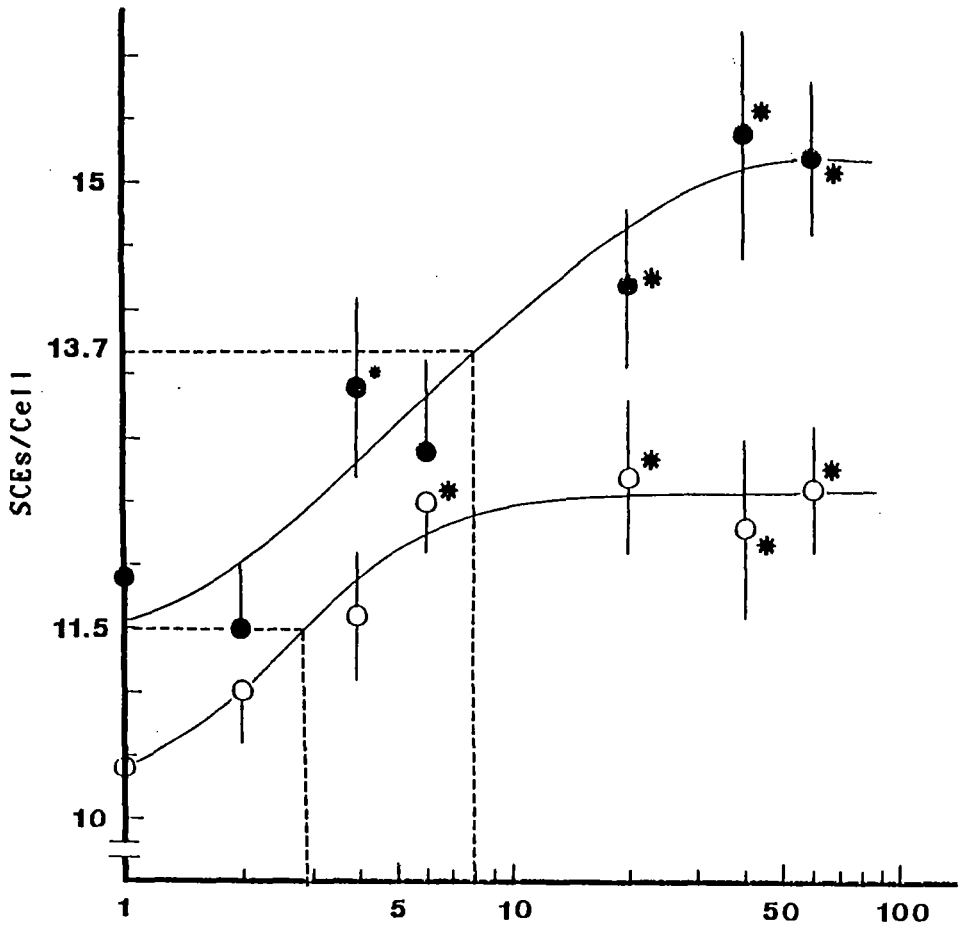

Fig.2. Effects of the mixture of PCDDs, PCDFs and Co-PCBs retained in healthy Japanese people on the induction of SCEs

○ : Mixture of PCDDs, PCDFs and Co-PCBs only

● : Mixture of PCDDs, PCDFs and Co-PCBs plus ANF(8×10^{-5}M)

* : $P<0.05$, ** : $P<0.01$