Damaging Effect of Organochlorine Chemicals to Hepatic DNA of Mice

KEIZO UMEGAKI, SACHIE IKEGAMI and TOMIO ICHIKAWA

The National Institute of Health and Nutrition,
Shinjuku-ku, Tokyo 162, Japan

Introduction

Various organochlorine chemicals are present in the environment such as pesticides, insecticides and intermediate products, and their carcinogenicity has not been fully elucidated. In this study the effects of organochlorine chemicals, mainly pesticides, on DNA single strand breaks (DNA SSB) and the formation of 8-hydroxy deoxyguanosine (8OH-dG) in DNA were examined in mice liver.

Methods

ICR mice (male, 6 weeks old, 5–6 mice per group) were daily administered (*per os*) organochlorine chemicals or a vehicle for 5 d. The daily dose of each chemical was about one-fifth of the reported LD₅₀. Mice were sacrificed after 4 h of the last administration. The examined chemicals were endrin, dieldrin, γ -BHC, chlorpyrifos, heptachlor, pentachloronitrobenzene, pp'-DDT, pentachlorophenol, chlordane, 2,4-d, mirex, pentachlorobenzene, hexachlorobenzene, chlorobenzilate, methoxychlor and trichloroethylene. As a positive control of hepatic DNA SSB, *N*-nitrosodimethylamine (NDMA) was also used. NDMA was administered as a single dose (20 mg/kg, *i.p.*) at 4 h before sacrifice. DNA SSB was analyzed by alkaline unwinding method¹⁾. Hepatic DNA was extracted and the content of 8OH-dG and dG in the DNA was measured by the method of Kasai *et al.*²⁾ using HPLC with an electrochemical detector and UV detector, respectively.

Result and Discussion

The administration of dieldrin, heptachlor, chlordane, mirex, pentachlorobenzene, hexachlor-

obenzene, chlorobenzilate, and trichloroethylene significantly increased liver weight. Hepatic DNA SSB in mice treated with trichloroethylene and pentachlorophenol was significantly enhanced, while the increase was much weaker than that in mice treated with NDMA. The value of % unwound DNA, which is increased by DNA SSB, was 8% in vehicle, 13% in pentachlorophenol, 14% in trichloroethylene and 45% in NDMA. The 8OH-dG level in hepatic DNA from vehicle-treated mice was 1.2 per 10⁵ dG and comparable with those of all groups chemically treated. These results suggest that the acute genotoxicity of the organochlorine chemicals tested in this study is rather weak.

References

- 1) S.R. Morris and H.G. Shertzer, *Environ. Mutagen.* **7**, 871 (1985).
- 2) H. Kasai, P.F. Crain, Y. Yuchino, S. Nishimura, A. Ootsuyama and H. Tanooka, *Carcinogenesis*, **7**, 1849 (1986).