Study on the Toxicity of 2,3,7,8-Tetrachlorodibenzo-*p*-dioxin (TCDD) Using Cultured Cells

Kohji TODOROKI, Shigeki SHIMBA, and Masakatsu TEZUKA*

Department of Hygienic Chemistry, College of Pharmacy, Nihon University, 7-7-1
Narashinodai, Funabashi, Chiba 274, Japan

Introduction

2,3,7,8-Tetrachlorodibenzo-*p*-dioxin (TCDD), a highly toxic compound that has recently attracted much attention as an environmental contaminant, elicits a variety of toxic responses. These include chloracne, tumor promotion, thymic involution, wasting syndrome, hydronephrosis and cleft palate.¹⁾ Although TCDD affects a wide variety of animal species *in vivo*, it is almost innocuous to several cultured mammalian cells in their proliferation and morphology.²⁾ Therefore, it seems necessary to establish an *in vitro* system that provides a model for studying the toxicity of TCDD. In this study, we examined the effects of this compound on cultured cell lines derived from its target tissues.

Materials and Methods

TCDD was purchased from GL Science (Tokyo, Japan). L-132 cells and BGM cells were plated at an initial density of 5×10^4 cells in MEM supplied with FBS in 35 mm tissue culture dishes. F9 cells were differentiated by the addition of 100 nM retinoic acid and 1 mM cAMP. 3T3 L-1 cells were subjected to differentiation experiments in Dulbecco's modified Eagle's medium (DMEM) containing 0.25 μ M dexamethasone, 0.5 mM isobutylmethylxanthine and 1.6 μ M insulin. Rat primary hepatocytes were prepared as described elsewhere.³⁾

Results

When L-132 cells derived from human embryonic lung were treated with 100 nM TCDD, the cell proliferation was significantly inhibited. The cell growth of kidney-derived BGM cells was also

suppressed by the addition of TCDD, but to a lesser degree than L-132 cells.

Since TCDD lowers the serum HDL level in humans, we wished to examine its effect on the secretion of HDL from rat primary hepatocytes. We found that secretion of HDL from TCDD-treated cells reduced to 75%.

TCDD is known to be a teratogen in several animal species, therefore, its effect on the differentiation of embryo cells was examined. F9 cells were treated with several different concentrations of TCDD in the presence of FBS. The treated cells were differentiated to parietal endoderm cells as were the control cells upon incubation with retinoic acid and cAMP.

The differentiation of the preadipose cells, 3T3 L-1 cells, was inhibited by the addition of 10 nM TCDD. Interestingly, the presence of insulin diminished the TCDD effects.

Discussion

To establish the systems that provide a model for the toxicity of TCDD, we chose several cell lines whose origins are target tissues of the compound. The present study indicates that rat primary hepatocytes and 3T3 L-1 cells are useful in the study of TCDD toxicity on the lipid metabolism and ultimately on wasting syndrome.

References

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