Significant Suppression of Aldolase B, Carbonic Anhydrase III and Alcohol Dehydrogenase in Liver Cytosol of Rats Treated with a Highly Toxic Coplanar PCB

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Introduction

Coplanar PCBs are extremely toxic chemicals which are widespread environmental pollutants and causal agents of Yusho. Toxic manifestation of coplanar PCB is thought to be mediated by aromatic hydrocarbon (Ah)-receptor. However, the relationship between the induction of gene expression *via* Ah-receptor and the toxicity has not been clearly understood. We theorized that there might be an important protein which has been unknown as inducible or suppressible with a toxic coplanar PCB. We found that 3,3',4,4',5-pentachlorobiphenyl (PenCB) strongly induces a 54-kDa protein in liver cytosol of rat, which is homologous to mouse 56-kDa selenium binding protein or acetaminophen binding protein,¹⁾ while, several cytosolic proteins were significantly suppressed by a coplanar PCB-treatment. We report here the identification of these suppressible proteins and propose new aspects of toxicity caused by toxic coplanar PCB.

Methods

Male Wistar rats were treated with PenCB (single 25 mg/kg, i.p.) as described previously.¹⁾ Free- and pair-fed control groups were treated with vehicle and cared for as described previously.¹⁾ At the day 5, the liver cytosol was prepared. The cytosolic proteins were compared among three groups by sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) and two-dimensional PAGE (2D-PAGE).

Results and Discussion

Expression level of cytosolic 40-kDa and

27-kDa proteins in rat liver were markedly suppressed by PenCB-treatment. The 40-kDa proteins were identified as aldolase B (Ald B) and alcohol dehydrogenase (ADH) class I by amino acid sequencing of the internal peptides. The 27-kDa protein was also identified as carbonic anhydrase III (CA III). The liver cytosolic Ald and ADH activities were significantly reduced to about 50% and 60% of both control groups by PenCB-treatment. Immunoblotting after 2D-PAGE demonstrated that Ald B was markedly suppressed by PenCB-treatment, while change in Ald A was slight.²⁾ The reduction of ADH by PenCB-treatment was also verified by immunoblotting. The significant suppression of CA III by PenCB-treatment in rat liver was demonstrated by immunoblotting using CA III-selective antibody. Ald plays an important role in glycolytic and gluconeogenic pathways. In addition, ADH catalyzes biotransformation of triose phosphate to glycerol-3-phosphate. Suppression of Ald B and ADH may be a key biochemical lesion for disordered intermediary metabolism occurring by PenCB-treatment and should be taken into account as a cause of the wasting syndrome which is a severe toxic effect of toxic coplanar PCBs. CA III possesses tyrosine phosphatase activity, therefore, its suppression could account for the effects on signal transduction by toxic coplanar PCBs.

References

- 1) Ishii Y., Hatsumura M., Ishida T., Ariyoshi N., Oguri K., *Toxicol. Lett.*, **87**, 1 (1996).
- 2) Ishii Y., Kato H., Hatsumura M., Ishida T., Ariyoshi N., Oguri K., *Toxicology*, in press.