Mechanisms of action and prediction of neurotoxicity for chemical substances

1988 Fiscal Year Final Research Report Summary

Mechanisms of action and prediction of neurotoxicity for chemical substances

Research Project

Project/Area Number

61480164

Research Category

Grant-in-Aid for General Scientific Research (B)

Allocation Type

Single-year Grants

Research Field

Hygiene

Research Institution

Dept. Hygiene, School of Medicine, Kanazawa University

Principal Investigator

HASHIMOTO Kazuo Dept. Hygiene, School of Medicine, Kanazawa University, 医学部, 教授 (30092795)

Co-Investigator(Kenkyū-buntansha)

SAKAMOTO Junko Dept. Hygiene, School of Medicine, Kanazawa University, 医学部, 助手 (90110626)
TANII Hideji Dept. Hygiene, School of Medicine, Kanazawa University, 医学部, 助手 (90110618)
HAYASHI Masao Dept. Hygiene, School of Medicine, Kanazawa University, 医学部, 助教授 (70164960)

Project Period (FY)

1986 – 1988

Keywords

Chemicals / Acrylamide derivatives / Inorganic metals / Neuronal cell culture / Structure-neurotoxicity / 構造一活性相関 / 神経毒性予測

Research Abstract

There have been many incidences of toxic neuropathies due to industrial chemicals environmental pollutants, drugs, insecticides and other chemicals. It is very important to prevent these diseases, since neuropathies are sometimes severe and irreversible. The present study was done to examine the mechanisms of neurotoxic action and to predict the neurotoxicity of chemicals. The results obtained are as follows:
1. It has been suggested that either the direct action to neurofilaments or to Ca^<2+> acitivated neutral protease is related to the neurotoxicity of chemicals.

2. Neurotoxic acrylamide derivatives inhibited dose-dependently the neurite outgrowth from retinal explant culture, but non-neurotoxic ones did not show any effect on the growth.
3. Neurotoxic acrylamide derivatives caused degeneration of mouse neuroblastoma cells and inhibition of cell growth, but only inhibition of cell growth in rat Schwannoma cells. These chemicals inhibited more the immature cells than the mature cells.
4. Growth of cerebellar astrocytes from rat embryo was dose-dependently inhibited by acrylamide derivatives, and the inhibition was postulated to be caused by that of cell division.
5. Protein content, lactic dehydrogenase activity and glucose consumption of neuronal cells from rat embryo were all inhibited dose-dependently by neurotoxic acrylamide derivatives. This culture system seems to be appropriate for neurotoxicity assessment.
6. Primary neuronal cell culture from rat embryo was vulnerable to acetaldehyde, which was the main metabolite of ethanol. The inhibitory effect of acetaldehyde was protected by thiol compounds such as reduced glutathione.
7. Inorganic metals inhibited dose-dependently growth of cultured neuronal cells and astrocytes. The effect was significantly correlated with chemical softness of the metals.

Research Products (13 results)

All | Other

All | Publications (13 results)

[Publications] Hideji Tanii: Archives of Toxicology. 61. 298-305 (1988)

[Publications] Masao Hayashi: Toxicology in Vitro. 2. 69-74 (1988)

[Publications] Hideji Tanii: Kazuo Hashimoto. 10(Suppl.). 209-218 (1988)

[Publications] Masao Hayashi: Archives of Toxicology.

[Publications] Kazuo Hashimoto: Proceedings of Medichem.

[Publications] Kazuo Hashimoto: "Seminars of Toxicity Mechanisms I" Center for Academic Publications, 126 (1987)

[Publications] Hideji Tanii: "Seminars of Toxicity Mechanisms I" Center for Academic Publications, 126 (1987)

[Publications] Hideji Tanii: "Cytotoxicity of acrylamide and related compounds to mouse neurobrastoma and rat Schwannoma cells" Archives of Toxicology. 61. 298-405 (1988)

[Publications] Masao Hayashi: "Effect of acrylamide on cerebellar astrocyte proliferation in vitro" Toxicology in Vitro. 2. 69-74 (1988)

[Publications] Hideji Tanii: "Neurofilament degradation in the nervous system of rats intoxicated with acrylamide; related compounds or 2,5-hexanedione" Archives of Toxicology. 62. 70-75 (1988)

[Publications] Kazuo Hashimoto: "Toxicological aspect of acrylamide neuropathy" J. Univ. Occup. Indust. Health. 10(Suppl). 209-218 (1988)

[Publications] Masao Hayashi: "Cytotoxic effect of acrylamide and its related compounds assessed by protein content, LDH activity and cumulative glucose consuption of neuron-rich cultures in a chemically defined medium" Archives of Toxicology.

[Publications] Kazuo Hashimoto: Seminars of Toxicity Mechanisms I. Center for Academic Publications Japan, 1-126 (1987)

URL: https://kaken.nii.ac.jp/report/KAKENHI-PROJECT-61480164/614801641988kenkyu_seika_hokoku_

Published: 1990-03-19