Short-Term Bioassays in the Analysis of Complex Environmental Mixtures IV

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FOREWORD

With this proceedings of the fourth symposium on complex mixtures, we continue to revise and extend our knowledge of genetic methods for the evaluation of chemical mixtures in the environment. The early chapters of this volume are devoted to new bioassay techniques that are directly applicable to the monitoring of environments contaminated with genotoxic chemicals. Microbiological methods have been further refined to meet the special needs of atmospheric monitoring so that very small samples may now be efficiently tested. New *in situ* methods utilizing green plants actually avoid many of the usual difficulties of sample collection and preparation and offer special advantages in monitoring wastewater, sludges, and hazardous wastes. Insects also are being employed very effectively in the evaluation of gaseous air pollutants in controlled laboratory investigations.

Increased emphasis has been placed on a comprehensive assessment of the potential of complex mixtures to cause various kinds of genetic damage. New assays for chromosome structural and numerical aberrations in mammalian cells *in vitro* have been developed and are being applied in laboratory studies. Efforts to link tests for gene mutation and cell transformation *in vitro* with assays for tumorigenesis *in vivo* are contributing to the validation of the short-term testing approach. Studies comparing *in vitro* and *in vivo* data on a coal conversion by-product, on polycyclic aromatic hydrocarbons, and on mineral fibers are reported in separate papers.

Later chapters are devoted to investigations on the fractionation and biological evaluation of specific chemical components within complex mixtures. Toward this end, it has been possible to generate complex atmospheres in which individual components are varied in concentration so that the biological consequences may be observed using microbial assays. Similar techniques have been used to demonstrate the formation of potent mutagens, the nitropyrenes, in environmental mixtures as well as in foods. The compound 1-nitropyrene was detected in cooked meat, but was not found to be carcinogenic in mice. On the other hand, the combustion emission constituent 1,6-dinitropyrene was clearly demonstrated to be a carcinogen in mice.

The effect of atmospheric transformation of automotive exhaust organics and of woodstove emissions has received much needed attention. Chamber studies showed that atmospheric processes can both increase and decrease the mutagenicity of emitted organic compounds. Atmospheric gases such as ozone and nitrogen oxides and physical factors such as light intensity and humidity dramatically modify the chemical transformation processes as monitored by analytical techniques and microbial assays.

Fractions of ambient air particulate extracts have been extensively studied in a major statewide sampling and analysis program. The results will provide reference points for future sampling and mutagenicity studies in other parts of the country. In another study involving five cities, inter-urban variations in the mutagenic activity of ambient aerosols were investigated in reference to fuel use patterns and seasonal variables. Mutagenic activities reflected differences in the chemical composition of the aerosols from the five cities studied; these differences, in turn, could be related to fuel use patterns. Similarly, the wastewaters and sludges of a major municipal treatment plant were impacted by industrial effluents and, again, microbial systems demonstrated their utility in municipal waste management.

The assessment of human health risk from complex mixtures of environmental chemicals remains a difficult problem. Definite progress has been made in the development and implementation of short-term tests that are directly applicable to the monitoring of individuals exposed to complex mixtures, especially in the workplace. The mutagenicity of urine has been studied as a non-specific indicator of exposure to genotoxic agents. Cytogenetic analyses of peripheral blood lymphocytes appear to provide a more direct biological measure of induced genetic damage in somatic cells. Studies are reported on pharmaceutical operations with cytostatic drugs, on formaldehyde in mobile homes, and on ethylene oxide in sterilization facilities. The latter study on ethylene oxide is the largest to date and clearly demonstrates that exposure to the compound is associated with an increase in sister chromatid exchanges in peripheral lymphocytes. Future investigations may be expected to monitor other types of genetic damage in lymphocytes, including specific gene mutation. The course of development of a clonal assay for gene mutation in human lymphocytes is described in detail. There has as yet been only limited use of such direct human monitoring approaches in mutagenesis or carcinogenesis risk assessment. Short-term genetic bioassay data, in the context of risk assessment, has been used principally to estimate comparative carcinogenic potency, as described in the last paper in the volume. This approach will be applied in the future to a wide variety of test data on complex mixtures.

Additional research must be performed to further characterize the nature and extent of genetic hazards posed by human exposure to complex chemical mixtures. Future volumes may be expected to provide a more exhaustive discussion of methods to integrate chemical analytical data with short-term test data and data obtained directly from human monitoring. In this way, methods for hazard identification may be extended in their utility, and risk assessment techniques may be refined by direct measurements of genetic damage in humans.

Michael D. Waters

CONTENTS

Keynote Address	3
Scott Baker	
SESSION 1: NEW DEVELOPMENTS AND TECHNIQUES.....	7
Use of the Microscreen Assay for Airborne Particulate Organic Matter*.....	9
Toby G. Rossman, LeRoy W. Meyer, James P. Butler, and Joan M. Daisey	
Development of an <i>In Situ</i> Test System for Detection of Mutagens in the Workplace*.....	25
Tong-man Ong, John D. Stewart, James D. Tucker, and Wen-Zong Whong	
Perturbations of Enzymic Initiation of Excision Repair Due to Guanine Modification in DNA [†]	37
Nahum J. Duker	
Plant Genetic Assays to Evaluate Complex Environmental Mixtures*	45
Michael J. Plewa	

*Invited paper.

[†]Based on poster presentation.

Studies with Gaseous Mutagens in <i>Drosophila Melanogaster</i>*	65
P.G.N. Kramers, B. Bissumbhar, and H.C.A. Mout	
Anaphase Aberrations: An <i>In Vitro</i> Test for Assessing the Genotoxicity of Individual Chemicals and Complex Mixtures*	75
Richard M. Kocan and David B. Powell	
Anaphase Aberrations: An <i>In Vivo</i> Measure of Genotoxicity*	87
Vincent M. Liguori and Marsha L. Landolt	
Measurement of Chemically Induced Mitotic Nondisjunction Using a Monochromosomal Human/Mouse Hybrid Cell Line*	99
Raghubir S. Athwal and Shahbeg S. Sandhu	
Toxicologic Responses to a Complex Coal Conversion By-Product: Mammalian Cell Mutagenicity and Dermal Carcinogenicity*	113
Michael L. Cunningham, David A. Haugen, Frederick R. Kirchner, and Christopher A. Reilly, Jr.	
Increased Virus Transformation by Formaldehyde of Hamster Embryo Cells Pretreated with Benzo(a)pyrene*	125
G.G. Hatch and T.M. Anderson	
Enhancement of Anchorage-Independent Survival of Retrovirus-Infected Fischer Rat Embryo Cells for Determining the Carcinogenic Potential of Chemical and Physical Agents†	139
William A. Suk, Joan E. Humphreys, E. Perry Hays, and John D. Arnold	
Correlation Between <i>In Vivo</i> Tumorigenesis and <i>In Vitro</i> Cytotoxicity in CHO and V79 Cells After Exposure to Mineral Fibers*	155
L.D. Palekar, B.G. Brown, and D.L. Coffin	

Quality Assurance and Good Laboratory Practice Regulations for Short-Term Bioassays of Complex Mixtures†	171
Robert S. DeWoskin	
Generation and Characterization of Complex Gas and Particle Mixtures for Inhalation Toxicologic Studies*	181
Michael T. Kleinman, Robert F. Phalen, and T. Timothy Crocker	
SESSION 2: INTEGRATED ASSESSMENT	193
Nitro Compounds in Environmental Mixtures and Foods*	195
Yoshinari Ohnishi, Takemi Kinouchi, Yoshiki Manabe, Hideshi Tsutsui, Hisashi Otsuka, Hiroshi Tokiwa, and Takeshi Otofujii	
The Effect of Atmospheric Transformation Upon the Bacterial Mutagenicity of Airborne Organics: The EPA Experience*	205
L.D. Claxton, L. Cupitt, R. Kamens, and L. Stockberger	
Mutagenicity Studies of New Jersey Ambient Air Particulate Extracts*	211
Thomas B. Atherholt, Gerard J. McGarrity, Judith B. Louis, Leslie J. McGeorge, Paul J. Liroy, Joan M. Daisey, Arthur Greenberg, and Faye Darack	
Interurban Variations in the Mutagenic Activity of the Ambient Aerosol and Their Relations to Fuel Use Patterns*	233
J.P. Butler, T.J. Kneip, F. Mukai, and J.M. Daisey	
Mutagenicity Analyses of Industrial Effluents: Results and Considerations for Integration into Water Pollution Control Programs*	247
Leslie J. McGeorge, Judith B. Louis, Thomas B. Atherholt, and Gerard J. McGarrity	

Isolation of Mutagenic Compounds from Sludges and Wastewaters*	269
M. Wilson Tabor, John C. Loper, Betty Lu Myers, Laura Rosenblum, and F. Bernard Daniel	
SESSION 3: RISK ASSESSMENT	289
Application of Short-Term Tests in Monitoring Occupational Exposure to Complex Mixtures*	291
Harri Vainio and Marja Sorsa	
An Integrated Approach to Human Monitoring*	303
Vincent F. Garry, Robert A. Kreiger, John K. Wiencke, and Richard L. Nelson	
Human Cytogenetic Monitoring: Occupational Exposure to Ethylene Oxide*	313
S.M. Galloway, P.K. Berry, W.W. Nichols, S.R. Wolman, K.A. Soper, and P.D. Stolley	
Direct Mutagen Risk Assessment: The Development of Methods to Measure Immunologic and Genetic Responses to Mutagens*	333
Gary H.S. Strauss	
Risk Assessment of Complex Mixtures*	353
Herman J. Gibb and Chao W. Chen	
Comparative Potency of Complex Mixtures: Use of Short-Term Genetic Bioassays in Cancer Risk Assessment*	363
Joellen Lewtas	
INDEX	377