Improving Bioaccumulation Assessment:  
Relationship Between In Vitro and In Vivo Biotransformation 
Rates of Hydrophobic Organic Chemicals in Mammals 

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Abstract 

The effective management of industrial and commercial chemicals in the environment requires good public policy based on sound science. The overall objective of this research is to improve national and international regulatory programs for the environmental management of industrial and commercial chemicals by developing and testing methods for the assessment of bioaccumulation of chemicals in biota. Bioaccumulation is a key consideration in the assessment of the environmental impacts of chemicals on environmental and human health. A review of regulatory approaches to the assessment and management of chemicals shows that current methods for assessing chemical bioaccumulation lack a priori consideration of the ability of organisms to biotransform chemicals and methods to assess bioaccumulation in species other than fish. The specific objective of my research is to develop and test a scientifically sound and cost-effective method for assessing bioaccumulation of chemicals in a mammalian species that incorporates the ability of mammals to biotransform chemicals. A thin-film sorbent-phase dosing method was developed and tested to measure the in vitro biotransformation rates of hydrophobic chemicals in rat and fish liver S9 fractions. The results showed that the biotransformation rates measured using the sorbent-phase dosing system were significantly higher than those measured using conventional solvent-delivery dosing methods. The sorbent-phase dosing system demonstrated several advantages over traditional solvent-dosing methods for hydrophobic chemicals by (i) eliminating incomplete dissolution of very hydrophobic substances in largely aqueous liver homogenates; (ii) providing a method for measuring the unbound fraction of substrate in solution; and (iii) simplifying chemical analysis. Also, an in vitro-to-in vivo extrapolation (IVIVE) method was developed to estimate whole body biotransformation rate constants and biomagnification factors (BMFs) of hydrophobic chemicals in rats from in vitro biotransformation rates. The IVIVE methodology was evaluated and found to be consistent with IVIVE models for pharmaceuticals and produced estimates of rat whole body biotransformation rate constants and BMFs for benzo[a]pyrene which were within the range of empirical values. The proposed IVIVE model for bioaccumulation assessment requires fewer physiological and physiochemical parameters than those used for pharmaceutical drug research; does not involve interconversions between clearance and rate constants in the
extrapolation; and may be a useful method for conducting regulatory bioaccumulation assessments in a mammalian species. Finally, recommendations for improving regulatory assessment and control of potentially hazardous commercial chemicals in Canada are presented.

Summary of Program of Study

- B.Sc., College of Nuclear Science, National Tsing Hua University, Taiwan (1996)
- M.Sc., College of Nuclear Science, National Tsing Hua University, Taiwan (1998)
- M.E.M. (Environmental Management), Nicholas School of the Environment, Duke University, USA (2002)
- Ph.D. Candidate, Resource and Environmental Management, Simon Fraser University, Vancouver, Canada (present)

Publications


Presentations


Statement of Interdisciplinarity

My research assesses the limitations of current regulatory management of industrial and commercial chemicals, develops scientific approaches to improve bioaccumulation assessment of chemicals, and provides recommendations for improving chemicals management in Canada. Therefore, my research integrates concepts from various disciplines, including public policy, ecology, environmental science, and environmental toxicology.