IN VITRO TOXICOLOGY

Environmental contaminants (Air, water and soil contaminants)

The quality of human life has been adversely affected by exposure to individual and complex exposures to contaminated media including: air, water and soil. Multiple exposures to a complex environment of hazardous chemicals, toxic gases, vapours, particulates and mixture of these can cause both acute and chronic adverse health effects but, the precise mechanisms that derive such effects are yet to be understood. Conventional animal based toxicity tests are expensive, time consuming, unable to evaluate multiple exposures and present challenges of interspecies extrapolation.

For many years, CSAT Labs has been involved in the development of alternative in vitro test methods for toxicity testing of a wide range of hazardous compounds in environmental media. For example, an integrated in vitro approach was designed for toxicity testing of airborne contaminants in which appropriate air sampling and exposure techniques were developed. Methods have been developed that involve the direct exposure of human cells to airborne contaminants by culturing cells on porous membranes. Once cells were established on membrane cells were directly exposed to airborne contaminants at the air/liquid interface which included the use of a horizontal diffusion chamber system for delivery of generated test atmospheres. Implementation of a range of in vitro bioassays in conjunction with innovative in vitro exposure techniques have been developed in this research can potentially provide an advanced technology for toxicity testing and biomonitoring of occupational and environmental airborne contaminants.

This area of research involves assessing the toxicity of a range of atmospheric and environmental contaminants including: workplace toxicants, air pollution, vehicle emissions, fire combustion products (using a pilot size furnace) and contaminated site assessment of air, water and soil.

Multiple chemical exposures

Despite the number of useful methods which have been developed for the assessment of toxicity of single chemicals, there is a very little information about evaluating the toxic effects of chemical mixtures. In the majority of cases people are exposed to mixtures of chemicals rather than single compounds. For example, solvent ex posures usually involve a mixture of chemicals. Although it is usually assumed that the toxic effects of multiple exposures are additive, chemicals may also interact synergistically or antagonistically. Exposure to multiple chemicals may induce a wide variety of toxic effects, even when single exposure levels are relatively low.

This area of research involves assessing the toxicity of a range chemicals and chemical mixtures with special interest in the Globally Harmonised System (GHS) of Classification and Labeling of Chemicals.

Cosmeceuticals/Pharmaceutical product safety using human skin *in vitro*

Skin is the largest organ of the body, consisting of composite layers (epidermis, dermis and hypodermis), different cell types (eg. keratinocytes, fibroblasts, melanocytes etc) each with specific structures and functions The skins major function is to protect the body from the

absorption of exogenous substances and microorganisms, to aid in thermoregulation and prevent water loss. Some substances can be absorbed by the skin in sufficient quantities to produce effects at both the cellular and tissue/organ level. These effects may be beneficial or harmful.

This area of research involves assessing the in vitro percutaneous absorption of test compounds for eg. cosmeceuticals and pharmaceutical through freshly excised human abdominal skin (elective surgery) using a Franz Diffusion Cell Apparatus (PermeGear). A histological assessment can also be performed on exposed skin discs to assess the degree of toxicity to skin at the cellular level by looking at a range of skin markers including antibodies.

CURRENT DIRECTION

Environmental contaminants (Air, water and soil)

To investigate the toxicity of airborne contaminants direct exposure methods were developed in CSAT labs using cultured cells on porous membranes. These human cells were directly exposed to airborne contaminants at the air/liquid interface. Toxicity of a range of airborne contaminants including: gaseous contaminants, vapours of volatile organic solvents and combustion products were investigated. Currently, the CSAT research group are interested in researching the potential of these test methods for the toxicity assessment of particulates including nanoparticles and ultrafine particles. As more nanomaterial products are brought to commercial use, the potential human adverse health effects need early investigation.

In vitro bioassays in conjunction with innovative exposure techniques have the potential to provide an advanced technology for toxicity testing and biomonitoring of occupational and environmental airborne contaminants. While the early laboratory based studies of complex atmospheres have been initiated at CSAT Labs in the area of fire combustion products, the problem of human airborne complex exposures has much broader aspects that need further investigations. Data derived from onsite toxicity investigations could potentially provide more representative information related to human complex exposures and may potentially be used to develop more accurate exposure standards for mixtures of airborne contaminants.

Multiple chemical exposures

Considering there are approximately 80,000 chemicals in commercial use, and an extremely large number of chemical mixtures, in vivo testing of this number of chemicals is unachievable from practical, ethical and economic perspectives.

Possible mechanisms of interaction between chemical mixtures have been investigated in several projects of the CSAT Labs. These research findings emphasise the importance of considering the possible interactions of chemical mixtures in future environmental and occupational toxicity assessments. This is importantant to avoid underestimation of toxic effects of chemical exposures.

Cosmeceuticals/Pharmaceutical product safety using human skin in vivo

This area of research offers the potential to determine what concentrations of test compounds eg. cosmeceuticals/pharmaceutical are safe for human topical exposure by generating risk assessment data for regulatory authorities, researchers and the consumers. This research enables a better understanding of the functioning of skin in response to topical exposure at both the tissue and cellular level. Research projects have included collaborations with the Australian company Ultraceuticals Pty Ltd where a immunohistological study of anhydrous ascorbic acid for therapeutic application to human skin was undertaken.

FUTURE PROJECTS

Environmental contaminants (Air, water and soil)
Vehicle emission, Volatile organic compounds, Fire combustion products, Contaminated site toxicity assessment, Workplace contaminants, Nanoparticles

Multiple chemical exposures
Assessing the toxicity of chemical mixtures, Toxicity assessment of environmental complex exposures, Industrial chemicals and commercial products

Cosmeceuticals/Pharmaceutical product safety
Therapeutic agents targeting particular skin markers, Safety assessment of formulated consumer product

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