Pharmacological and Toxicological Characterization of NHP Ingredients and Product Formulations

NRC·CNRC

Aquatic and Crop Resource Development

Scientific Application to Natural Health Products

The Natural Health Products (NHP) Program offers non-GLP ADME, pharmacological and toxicological solutions to enable ingredient and product development and reduce product development timelines.

Technical Capabilities

Analytical

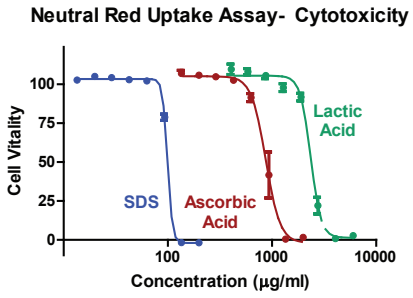
- Advanced support of pre-clinical testing of ingredients and product formulations using HPLC, LC-MS, GC-MS and NMR

High Content Screening Assays (ImageXpress Micro XL)

- Bioactivity discovery, efficacy and safety assessment using high-throughput and automated cellular imaging[1]

Cytotoxicity of Ingredients in Cell Based Assays

- Neutral Red Uptake assay in 3T3 cells (OECD/ICCVAM method)
- Neutral Red Uptake assay in HepG2 (human liver cells)
- Phototoxicity testing by Neutral Red Uptake[1]



Concentration response curves showing cytotoxic effects of tested materials. Curves to the right indicate less cytotoxicity.

Metabolic Stability

- Ingredient stability in rat and human microsomes and primary human hepatocytes
- Ingredient metabolite identification and profiling

1-Capabilities under development

National Research Council Canada
Conseil national de recherches Canada
Canada

Aquatic and Crop Resource Development

Neutral Red Uptake Assay- Cytotoxicity			
Test material	**NRC-EC_{50} (µg/ml)**	**SD multiple experiments**	**IC_{50} (µg/ml) literature values**
SDS	98	2	90 to 93
Lactic acid	2351	103	1560 to 4160
Ascorbic acid	822	83	490 to 810
EDTA	560	14	500 to 950
Colchicine	0.025	0.004	0.018 to 0.046

*EC_{50} Effective Concentration to kill 50% of cells. Higher EC_{50} values indicate less cytotoxic compounds. NRC test results are shown in comparison reference literature values.

Bioavailability

- Absorption studies in intestinal models- PAMPA assay and $CaCo_2$ cells
- In vivo rodent models

PK/PD Studies

- Dose optimization and formulation testing

Drug-drug Interaction Studies

- Mouse, rat and human microsomal P450 inhibition
- Human liver P450 induction (HepG2 and primary human hepatocytes)
- Custom in vivo drug-drug interaction studies

Efficacy Studies in Pre-clinical Disease Models

- Dyslipidemia, diabetes and obesity models
- Tumour implant models
- Contact for other models

In vivo Safety

- Custom rodent toxicology studies
- Rodent telemetry studies- Cardiovascular and neurological safety

Specific Areas of Expertise

- Ingredient and formulation safety and efficacy evaluation
- In vitro and in vivo bioavailability studies
- Product differentiation studies (bioavailability and efficacy)
- Pre-clinical evaluation in cell based and in vivo models
- Dose optimization and determination of safety window
- Safety assessment – Cytotoxicity, phototoxicity, drug-drug interactions, in vivo telemetry, non-GLP in vivo toxicology

Get started today

Have our Client Relationship Leader meet with your scientific and management teams to match NRC capabilities to your needs.

Contact

Business Related Inquiries:
Jason Steele
Client Relationship Leader
Tel: (902) 402-1714
jason.steele@nrc-cnrc.gc.ca
www.nrc-cnrc.gc.ca

Technical Related Inquiries:
Jeff Chisholm
Research Officer
Tel: (902) 367-3378
jeff.chisholm@nrc-cnrc.gc.ca
www.nrc-cnrc.gc.ca

March 2013 Également disponible en français.