

## Phytotherapy-induced hepatocytotoxicity

Manuela Neuman, Yaacov Maor, Marius Braun, Ana Tobar, Ehud Melzer and Stephen Malnick  
University of Toronto, Canada

**Background & Aims:** Herbal medicine is frequently integrated with conventional medicine. We report a case of severe-herbal-induced liver injury (HILI) due to Herbalife tea and protein-shake. We present both clinical and laboratory evidence implicating an immune response leading to a hypersensitivity reaction.

**Methods:** A 65 year old lady was hospitalized due to progressive jaundice and hepatocellular injury. 6 months previously she noted lassitude and disturbed liver enzymes were detected. Due to the appearance of deep jaundice she was hospitalized. On repeated history ingestion of Herbalife tea and protein-shake was noted. Liver biopsy revealed necrotizing granulomatous hepatitis, apoptotic cells. PAS diastase stain was showing cluster of foamy macrophages with ceroid pigment, characteristic of toxicity. Immunohistochemistry demonstrated and bile duct loss (attached). Discontinuation of the Herbalife, and treatment with both prednisone and urso-deoxycholic acid resulted in slow resolution of her complaints (the ALT decreased from 1096 U/L to 69U/L and the GGT decreased from 899 to 218 U/L, but relapsed on 10 mg daily of prednisone (ALT increased to 246). Retreatment with both prednisone and azathioprine resulted in remission (ALT 41 and GGT 49 U/L). A lymphocyte toxicity assay (LTA) was performed. LTA % toxicity was: protein alone 20; tea alone 44; protein+ tea 66. The proinflammatory cytokines and chemokine (x control) in serum were elevated as follow: TNF (tumor necrosis factor alpha) x40; IL1 (interleukin) 12; IL6-x1.2; IL13-x3; IL8-x5. Vascular endothelial growth factor was 5106 pg/mL (x46). Mitochondrial markers M30 and M65 revealed


a predominant level of necrosis process versus apoptosis. The severe HILI resulting from the protein and herbal tea is consistent with a cholestatic picture. This is the first report of the cytokine disturbances associated with HILI from the combination of tea and shake protein (Herbalife). Moreover this is a clear demonstration of hypersensitivity-induced lymphocyte death linked to the same product combination.

**Conclusions:** In susceptible individuals protein and herbal tea might produce a strong T1 response leading to HILI. This finding is consistent with the majority of reports of Herbalife toxicity in the literature being due to the combination of protein shake and tea consumption.

### Speaker Biography

Manuela Neuman teaches clinical and experimental toxicology and pharmacology at the University of Toronto, Medical School, Canada. Dr. Neuman supervised several M.Sc., and Ph.D. theses as well as post-doc fellows and research projects for Medical Physicians. She is also in charge with Ph.D. international students (Cuba, Israel, Romania, France, Australia, South Africa) as well with Pharmacy and Medicine exchange M.Sc., international students from France and Medical fellows from Israel, Brazil, Cuba, Romania and Argentina. She is the founder of the In Vitro Drug Safety and Biotechnology. She is the head of In Vitro and of the biomarkers platforms at the University of Toronto. The role of micro quantitative liver function based upon mitochondrial activities; non-invasive biomarkers of fibrosis, inflammation and repair, immuno-pharmaco-genetics are subject of her research. She also explores biomarkers such as immuno-genomics and metabolomics as individual variation in personalized medicine approaches. Neuman studies the role of microbiota in the development of non-alcoholic liver disease as well as in severity of inflammation and its possible repair. This includes translational research that characterize, obesity, non-alcoholic fatty liver disease and non-alcoholic steatohepatitis. The recognition of the key role played by lipotoxicity in cellular injury and stimulation of the inflammatory responses leading to fibrogenesis is key for therapies.

e: m\_neuman@rogers.com

 Notes: