Assessment of Interactions Between Synthetic Xenoestrogens and Dietary Phytoestrogens: A Focus on Real World Mixture Exposures

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The major thrust of our research has been to develop statistical and experimental approaches that incorporate critical features of “real world” chemical mixtures, so that the mixture toxicity data are relevant to human risk assessment. These factors include moving beyond binary studies by increasing the number of chemicals in the mixtures, utilizing realistic mixing ratios, and focusing on the low dose region of dose-response curves. The current project will examine interactions within mixtures containing 3-6 synthetic xenoestrogens, and will examine how the toxicity of such mixtures is influenced by changes in the background level of dietary phytoestrogens. The mixtures will be assessed in a battery of assays including ER-α and ER-β reporter gene assays, a rat uterotrophic assay, and gene expression analysis of estrogen-responsive genes in selected tissues. Statistical analysis will compare the observed responses to those expected under the assumption of additivity. If possible, a threshold model will be used, since a key aspect of risk assessment is whether or not response thresholds shift when chemicals are combined. The benefits of the research will be to advance statistical techniques and experimental designs to deal with larger numbers of mixture components, and to inform some of the default assumptions likely to be used when assessing the combined toxicity of synthetic xenoestrogens. An examination of changes at the molecular level (e.g., gene expression) will also provide mechanistic data to support such assumptions. An initial two-year project has been completed, with a two-year renewal currently undergoing review.

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