RTI Prominent Publications Summary

Role of CYP2E1 in the Epoxidation of Acrylamide to Glycidamide and Formation of DNA and Hemoglobin Adducts

Ghanayem, B.I., McDaniel, L.P., Churchwell, M.I., Twaddle, N.C., **Snyder, R.**, **Fennell**, **T.R.**, & Doerge, D.R. (2005). Role of CYP2E1 in the epoxidation of acrylamide to glycidamide and formation of DNA and hemoglobin adducts. *Toxicological Sciences* 88 (2):311-318.


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Acrylamide, a known carcinogen, neurotoxin, and reproductive toxin, is an important industrial chemical used in the manufacture of paper, textile, and cosmetics. A decade ago, acrylamide was found in fried or baked carbohydrate-rich foods, heightening the concern of exposure to humans. Much of our understanding of the toxicity of chemicals is derived from testing conducted in rodents. An improved understanding of the fate of acrylamide and the role of specific enzymes in the metabolism of acrylamide was important to enable extrapolation of the findings in rodents to the potential dietary exposures in humans.

It has been well established that glycidamide, the reactive metabolite of acrylamide, binds to DNA and that this binding may be responsible for the mutagenicity and carcinogenicity of acrylamide. Previous studies had shown that the metabolism of acrylamide to glycidamide in mice required the CYP2E1 enzyme.

This paper demonstrated that exposure of wild type mice to acrylamide resulted in the formation of DNA adducts and hemoglobin adducts derived from acrylamide and glycidamide. However, in CYP2E1 null mice lacking this enzyme, similar administration of acrylamide resulted in DNA adducts that were 55- to 66-fold lower than in the wild type mice. Adducts derived from glycidamide in hemoglobin were approximately 33-fold lower in the CYP2E1 null mice compared with the wild type mice. By using mice lacking the CYP2E1 enzyme, we were able to confirm that this enzyme is responsible for the metabolism of acrylamide to glycidamide, and to demonstrate substantial differences in the formation of DNA and hemoglobin adducts derived from glycidamide.

Link: http://toxsci.oxfordjournals.org/content/88/2/311.full.pdf