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## Gerhard Eisenbrand

University of Kaiserslautern, Germany

### Low dose effects of the dietary carcinogen acrylamide

Acrylamide (AA) forms in food by thermal treatment from different precursors. AA undergoes partial bioactivation into the genotoxic metabolite glycidamide (GA), which binds to DNA, forming covalent adducts primarily at N7 of guanine (N7-GA-Gua). AA and GA undergo conjugation to glutathione (GSH), to be excreted *via* urine as mercapturic acids (MA), N-acetyl-S-(2-carbamoyl-ethyl)-cysteine (AAMA), and N-acetyl-S-(2-hydroxy-2-carbamoyl-ethyl)-cysteine (GAMA). In an extended dose response study from 0.1 µg up to 10 mg/kg bw, rats were gavaged with single dose of AA in water. Urinary MAs and N7-GA-Gua DNA adducts in liver, kidney and lung were measured 16 h later (C<sub>max</sub> of N7-GA-Gua). The control group excreted AA-related MAs in the urine at a level indicating some endogenous AA background formation. At lowest dosage (0.1 µg AA/kg bw), MA excretion and N7-GA-Gua adduct level were not found enhanced. At tenfold higher dosage (1 µg/kg bw), adducts were found in kidney (about 1 adduct/10<sup>8</sup> nucleotides) and lung (<1 adduct/10<sup>8</sup>). At 10 and 100 µg/kg bw, adducts were found in all three organs examined, at levels not significantly different from those found at 1 µg AA/kg bw (about 1-2 adducts/10<sup>8</sup>). The results indicate dose dependent DNA damage becoming measurable at dosages >100 µg/kg bw, not below (LOD 0.2 adduct/10<sup>8</sup>). Thus, exposure of rats to single dose of AA in the range of human dietary exposure (0.1-10 µg/kg bw) results in adduct levels in the range of steady state background DNA lesions associated with endogenous/exogenous exposure to various DNA damaging agents.

### Biography

Gerhard Eisenbrand is Professor Emeritus at the University of Kaiserslautern, Department of Chemistry, Division of Food Chemistry and Toxicology. His research was published in more than 350 peer reviewed scientific publications. He mainly focuses on mechanisms of actions of (geno) toxic and various anticancer agents, metabolism and biokinetics, recent and current research interactions of food constituents/contaminants with biomolecules in the organism, within the context of food safety and beneficial/ adverse effects relevant to human health, in experimental and human intervention studies. He was long acting (1995 to 2013) Chair of the Senate Commission on Food Safety (SKLM) of the German Research Foundation (DFG) and is currently Scientific President of ILSI Europe.

[eisenbra@rhrk.uni-kl.de](mailto:eisenbra@rhrk.uni-kl.de)