
The effects of allyl sulfides on the induction of phase II detoxification enzymes and liver injury by carbon tetrachloride.

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Abstract

Allyl sulfides, e.g., diallyl sulfide (DAS), diallyl disulfide (DADS), and diallyl trisulfide (DATS), are principal constituents of garlic oil. In the present study, we investigated the in vivo effect of these sulfides on the phase I and phase II drug-metabolizing enzymes, and elucidated their structure-function relationship. A highly purified form of each sulfide (more than 99% purity) was administered i.p. as a bolus to rats at a concentration of 10 or 100 micromol/kg body weight for 14 consecutive days. As to the phase I enzymes, DAS (100 micromol/kg) slightly but significantly increased cytochrome P-450 (CYP) 2E1 activity (1.6-fold vs. control), whereas DADS and DATS did not affect it or the hepatic total CYP level or CYP1A1/2 activity. With respect to the phase II enzymes, DATS (10 micromol/kg) and DADS at a 10-fold higher dose (100 micromol/kg) significantly increased the activities of glutathione S-transferase, quinone reductase, and antioxidative enzyme glutathione peroxidase; whereas DAS did not. In the carbon tetrachloride (CCl4)-induced acute liver injury model of rats, either DATS (10 micromol/kg) or DADS (100 micromol/kg) significantly reduced the injury caused by the induction of phase II enzymes with CCl4. In conclusion, the sulfides affected both phase I and phase II enzymes, the former being stimulated by the monosulfide only and the latter, strongly by the trisulfide and weakly by the disulfide. Therefore, the polysulfide DATS may be one of the important factors in garlic oil that protects our body against the injury caused by radical molecules encountered in daily life.

PMID: 15046820 [PubMed - indexed for MEDLINE]

Publication Types, MeSH Terms, Substances

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