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IN VITRO AND EX VIVO METABOLISM OF DIALLYL DISULFIDE, A CHARACTERISTIC SULFUR COMPOUND OF GARLIC, IN RAT.

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Many carcinogenesis studies have pointed out the chemoprotective effects of garlic. diallyl disulfide (DADS), a flavour compound of garlic, has been shown to protect liver from carcinogenesis induced by various chemicals. To identify the real active molecules, *in situ*, after ingestion of garlic, metabolism of DADS has been studied *in vitro* and *ex vivo* in an isolated perfused rat liver. *In vitro*, DADS in presence of microsomes was oxidised to only one metabolite, namely allicine (or DADSO). In rat microsomes, the reaction followed Michaelis-Menten kinetics with a $K_m = 0.86 \pm 0.1$ mM and a $V_{max} = 0.85 \pm 0.2$ nmol/min/pmol CYP. The action of phase II enzymes on DADS metabolism was studied by incubating DADS or DADSO with liver cytosols or microsomes. Two metabolites were formed from DADS: allyl glutathione sulfide conjugate and allyl mercaptan, whereas with DADSO, only the glutathione conjugate was observed. No conjugate compound was detected in the presence of UDP-glucuronyl transferases. *Ex vivo*, when isolated rat liver was perfused with DADS, different metabolites were obtained in the output and in the liver. These metabolites are being identified presently. The pharmacokinetic parameters indicated a rapid disappearance of DADS in this tissue, with little storage.