The present results show that DDC, like disulfiram, inhibits the hydroxylation of amphetamine and as a consequence increases the concentrations of amphetamine in brain and plasma. Several reports have appeared showing that amphetamine-induced stereotyped behaviour is prolonged after pretreatment with DDC in mice and rats (Randrup & Scheel-Krüger, 1966; D'Encarnacao, D'Encarnacao & Tapp, 1969; Mayer & Eybl, 1971). This effect of DDC has been interpreted as a result of inhibition of dopamine-β-hydroxylase leading to a decreased synthesis of noradrenaline and increased levels of dopamine in the brain Scheel-Krüger & Randrup, 1967; Mayer & Eybl, 1971). In view of the present findings the increased intensity and the prolongation of the amphetamine-induced stereotyped behaviour in DDC pretreated rats may better be explained by increased tissue levels of amphetamine. However, our data do not rule out the earlier conclusion, that the stereotyped behaviour is dependent on an intact dopaminergic transmission in the central nervous system.

Ethanol also caused an increase in the concentrations of amphetamine in the brain and plasma (Fig. 1b) as might be expected. This result is in agreement with the finding by Creaven & Barbee (1969), that ethanol is an inhibitor of the *p*-hydroxylation of amphetamine in the rat.

Further experiments are needed before the mechanisms of inhibition of amphetamine hydroxylation caused by DDC, ethanol and several other chemical agents (cf. Lewander & Jonsson, 1972) can be established.

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Deacetylation of acetyl sulphapyridine in man

It has been demonstrated that sulphapyridine, like isoniazid, sulphadimidine, and other drugs, is polymorphically acetylated in man (Schröder & Evans, 1972). Sulphapyridine and acetyl sulphapyridine are also subject to ring hydroxylation, the products being recovered in serum and urine as *O*-glucuronides. The further possibility remains, however, that acetyl sulphapyridine like monoacetyl dapsone (Gelber, Peters & others, 1971) also undergoes deacetylation in man.

Deacetylation can, in theory, be effected by the reversible action of the polymorphic N-acetyl transferase enzyme. However, it has been demonstrated that acetyl sulphadimidine is not deacetylated in man (Gelber & others, 1971), nor is acetyl isoniazid deacetylated by the partially purified enzyme (Jenne, 1965). It seems more likely that the deacetylation is effected by specific arylacylamidases (Weber, 1971).

Table 1. Urinary excretion of sulphapyridine and acetylsulphapyridine metabolites.

	Acetylator phenotype Slow (n = 5)	Rapid (n = 5)	t	*P*
Sulphapyridine (oral)				
% Acetylated drug in urine	42·0 ± 4·0	76·5 ± 5·6		
% *O*-Glucuronidized drug in urine..	59·8 ± 6·2	55·9 ± 8·7	1·01	N.S.
Total excretion % of dose	3·4 ± 1·7	5·7 ± 1·2	3·07	0·015
Acetyl sulphapyridine (oral)				
% Deacetylated drug in urine ..	9·4 ± 1·8	6·9 ± 1·3	3·24	0·012
% *O*-Glucuronidized drug in urine..	69·5 ± 3·5	61·6 ± 13·9	1·53	N.S.
Total excretion % of dose	4·4 ± 0·5	4·6 ± 2·5	0·25	N.S.

(Mean ± 95% confidence limits).
Student's *t*-test. N.S. = Not significant, $P > 0{\cdot}05$.

To study whether deacetylation of acetyl sulphapyridine occurs, 10 healthy volunteers were first phenotyped as slow or rapid acetylators according to the procedure by Schröder & Evans (1972) which was, however, modified such that only the urine formed between 7 to 8 h after ingestion of sulphapyridine (10 mg kg^{-1}) was collected. One week later, the experiment was repeated with an equimolar dose of acetyl sulphapyridine.

The results show that the sample consisted of 5 slow and 5 rapid acetylators. After ingestion of acetyl sulphapyridine, sulphapyridine was excreted in the urine. The slow and rapid acetylators differed significantly in their deacetylating capacities. In the slow acetylators the amounts of the deacetylated drug appearing in the urine were larger (see Table 1). The difference observed between slow and rapid acetylators in deacetylation could be caused by a more rapid reacetylation by the rapid acetylators.

After administration of both sulphapyridine and acetyl sulphapyridine, considerable hydroxylation of the drugs occurred (see Table 1). A larger proportion was hydroxylated after administration of acetyl sulphapyridine than after sulphapyridine, the difference between the drugs being significant ($P < 0{\cdot}001$). Hence rapid acetylators who are forming more acetyl sulphapyridine, should be expected to convert a larger proportion of sulphapyridine into hydroxylated metabolites than the slow acetylators. However, this study shows that both phenotypes hydroxylated similar proportions of sulphapyridine (see Table 1).

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