the rate of $^{14}CO_2$ formation nearly 70 per cent from [6-^{14}C] glucose and only 30 per cent from [1-^{14}C]glucose. These results have been interpreted as evidence for the lack of inhibitory action of ethanol on $^{14}CO_2$ derived from labeled glucose via the shunt pathway. The readiness with which NAD rather than NADP is reduced by ethanol in liver has been recently demonstrated.[9,10]

The earliest observation that NADP is an additional cofactor for ADH comes from the work of Pullman *et al.*[11] However, NADP has been shown to have 100 times less affinity than NAD for horse liver ADH, and 30 times less affinity for monkey liver ADH.[2] Furthermore, Dalziel and Dickinson[12] have demonstrated that NAD is firmly bound to ADH and competes with NADP. In view of this kinetic evidence, it is doubtful whether ethanol reduces NADP in preference to NAD and whether the small reduction of NADP is of any consequence in the operation of the hexose monophosphate shunt. A microsomal enzyme system which can reduce NADP in the presence of ethanol is present in the liver, but it requires high concentrations of NADP and ethanol, and is not likely to be of any physiological significance, according to Krebs and Perkins.[10] That the degree of inhibition of incorporation of the labeled amino acid into proteins by ethanol is parallel to the inhibition of $^{14}CO_2$ yields from [6-^{14}C]glucose rather than to that from [1-^{14}C]glucose is further evidence that the major pathways affected are glycolysis and the citric acid cycle, and not HMP. At high concentrations, it appears that ethanol inhibits macromolecular synthesis, probably by interfering with energy metabolism.[8] Therefore, the inhibition of nucleic acid and protein synthesis by ethanol noted by Beaconsfield and Reading[1] is likely due to the general depressant effect of ethanol on cellular mechanisms.

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Transport of isoniazid across rat small intestine *in vitro*

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MOST drugs are transferred across the mucosa of the gastrointestinal tract as unionized molecules. Rates of transfer are related to the proportion of unionized molecules and their lipid solubility.[1] Using everted sacs of rat small intestine[2] isoniazid transport was investigated *in vitro*. Isoniazid was measured by a semi-specific colorimetric method.[3]

At an initial concentration of 5 mM, on both sides of the everted sac, isoniazid was not transported against a concentration gradient. The concentration ratio (serosal conc./mucosal conc.) was 0·89 ± 0·007 S.E.M. for eight sacs from four rats.

Transfer of isoniazid with the concentration gradient was linear with initial concentration in the range of 0–15 mM. Uptake rates were as follows; 5 mM, 2·56 ± 0·33 S.E.M.; 10 mM, 4·93 ± 0·28 and 15 mM, 6·72 ± 0·20 μmoles/g wet wt./hr. The total recovery of isoniazid from the serosal and mucosal fluids was 95, 94 and 91 per cent respectively, suggesting a negligible metabolic loss of the drug. The sac tissue itself was not analysed for isoniazid. The presence of structural analogues, or metabolic inhibitors, did not alter transfer rates with this intestinal preparation (Table 1).

TABLE 1. EFFECT OF POSSIBLE INHIBITORS ON THE TRANSPORT OF 15 mM ISONIAZID ACROSS EVERTED SACS OF RAT SMALL INTESTINE

Possible inhibitor	Rates of transference μM/g wet wt/hr Mean ± S.E.M.		$\frac{\text{Test}}{\text{control}} \times 100$
	Control (no inhibitor)	Test (+ inhibitor)	
15 mM Nicotinic acid	8·72 ± 0·39	9·19 ± 0·71	105
15 mM Isonicotinic acid	13·9 ± 1·7	17·3 ± 1·2	125
15 mM Sodium azide	8·9 ± 0·88	10·8 ± 1·2	121

Six sacs, from three different rats, were taken for each control and for each test.

The results of our experiments *in vitro* may be compared with published results of *in vivo* studies. Absorption of isoniazid from perfusion of the small intestine of anaesthetized rats was linear with the initial concentration of the drug.[4] *In vivo* perfusion studies also showed poor absorption from rat stomach compared with rapid absorption from the small intestine.[5] By contrast, it appears that isoniazid does not penetrate circulating erythrocytes from analyses on plasma and whole blood of rabbits receiving isoniazid orally.[6]

From a study of blood levels in the human, after oral dosage, isoniazid seems to be absorbed very rapidly from the gastro-intestinal tract *in vivo*.[7] It is considered that isoniazid is probably absorbed throughout the whole length of the human intestine and probably even from the colon and rectum.[8,9]

Our results suggest that isoniazid is transferred across rat small intestine at pH 7·4 by passive diffusion *in vitro*.

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