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The Metabolism of [³⁵S]Homosulphanilamide

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Homosulphanilamide (4-aminomethylbenzenesulphonamide) is a valuable antibacterial drug when used topically for burns (Lindberg, Moncrief, Switzer, Order & Mills, 1965). Systemically it is ineffective because it is rapidly converted into the inactive 4-carboxybenzenesulphonamide (Hartles & Williams, 1947). The renewed therapeutic interest in this drug caused us to reconsider its metabolism, in particular the possibility of its deamination by the intestinal tissues.

[³⁵S]Homosulphanilamide was administered orally (50mg/kg) to the rhesus monkey, rat, guinea pig and rabbit, and two metabolites apart from the unchanged drug were found in the urine. These were 4-carboxybenzenesulphonamide and 4-acetamidomethylbenzenesulphonamide, the latter being shown to be a metabolite for the first time. In the monkey, guinea pig and rabbit the major product was 4-carboxybenzenesulphonamide (70–90% of the 24h excretion) with smaller amounts of the free and the acetylated drug. In the rat, however, the outputs of total homosulphanilamide and 4-carboxybenzenesulphonamide were approximately the same. The drug was thus less readily deaminated in the rat than the other species.

Homosulphanilamide is a substrate for monoamine oxidase (Beyer & Govier, 1945; Blaschko & Duthie, 1945), which is present in both liver and intestine. Therefore the effect of route of administration on the deamination of the drug was examined. The amount of 4-carboxybenzenesulphonamide excreted in the 24h urine in the rabbit (50% of dose) and rat (30% of dose) was the same whether [³⁵S]homosulphanilamide (500mg/kg) was administered orally or intravenously. This suggests that the intestine may not play a major role in deaminizing the drug.

The metabolism of the ³⁵S-labelled drug was studied in rabbits and rats pretreated with the monoamine oxidase inhibitor iproniazid (1-is-

nicotiny-2-isopropylhydrazine; Marsilid). In the rabbit the rate of excretion of ³⁵S was increased by about 25% by pretreatment, but in the rat it decreased by 25%. In both species the excretion of 4-carboxybenzenesulphonamide was markedly depressed and there was a corresponding increase in the excretion of total homosulphanilamide. Various combinations of oral and intravenous administration of homosulphanilamide and iproniazid were tried in an attempt to obtain information about the role of the gut compared with the other tissues in deaminating the drug, but no definite conclusions could be drawn from the results. It appeared that the drug was deaminated mainly by the liver rather than by the intestine.

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Protection by Zinc Ions against the Toxicity of Cadmium Ions

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Although Zn²⁺ is known to protect against the selective injurious effect of Cd²⁺ on the rat testis (Pařizek, 1960; Kar, Das & Mukerji, 1960; Gunn, Gould & Anderson 1961; Mason & Young, 1967), the mechanism of this protection has not been established. It seems unlikely that this is due to inhibition of the displacement by Cd²⁺ of Zn²⁺ from metalloenzymes, a possibility considered by Pařizek (1960), since the primary action of Cd²⁺ appears to be on the vascular system (e.g. Clegg, Carr & Niemi, 1969). The amount of Cd²⁺ accumulated by the rat testis is small (e.g. Pařizek, 1960) and does not lead to displacement of Zn²⁺. Indeed, the testicular content of Zn²⁺ remains unaltered for 48h after injection of Cd²⁺ (2.2 μmol/100g body wt.) and then increases to a value 9–10-fold greater than normal at 30 weeks.

In contrast with the testes, appreciable amounts of the injected Cd²⁺ accumulate in the livers and kidneys, this accumulation being accompanied by increases in the contents of Zn²⁺. In both tissues most of the bound Cd²⁺ is found as a single fraction in the cell sap, which also contains Zn²⁺. These proteins, in which the cations are bound at thiol groups, are not identical, but have properties in

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