these effects of zinc and ouabain are mutually additive, and those of the zinc, like those of the ouabain, are prevented by the same complexing agents. Phenanthroline is preferentially soluble in lipids, whereas the sulphonated derivative is preferentially soluble in water. Because the former is a much more effective antagonist of the ouabain contracture than is the latter, it is concluded that its site of action is separated from the bath fluid by a lipid membrane.

In 1964 Daniel showed that concentrations of ouabain sufficient to produce contracture also caused downhill ion movements of sodium and potassium. Concentrations of ouabain or of zinc, sufficient to cause potentiation of responses to other agonists, however, do not cause these downhill ion movements or inhibition of a sodium activated membrane ATPase, nor does the ouabain cause net movements of Ca or Mg.

The present data indicate clearly a relationship between the contractures and the potentiations produced by zinc and ouabain which is inconsistent with either being caused by inhibition of membrane ATPase. Both zinc and ouabain contractures and potentiations are inhibited by concentrations of adrenaline which are without effect on responses to acetylcholine. As adenyl cyclase is inhibited by zinc (Sutherland, Rall & Menon, 1962) and by ouabain (Ho, Jeanrenaud, Posternak & Renold, 1967), whilst it is activated by adrenaline (Sutherland & Rall, 1957), it is possible that these effects of ouabain and zinc are caused by inhibition of this enzyme, which, in turn, affects internal calcium release and contracture.

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Sodium maleate-induced potentiation of the penicillamine effect on the urinary mercury excretion

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Sodium maleate, which produces metabolic changes in the renal cells, has been shown to decrease the kidney mercury content and to increase the urinary mercury excretion, the lowest effective dose being 100 mg/kg s.c. (Clarkson & Magos, 1967). As it is a thiol reagent, experiments were carried out on albino rats to see whether sodium maleate modified the effect of some known thiol complexing agents on the urinary excretion of mercury.

It was found that sodium maleate enhanced the effect of *d*-penicillamine, and to a lesser extent that of *N*-acetyl-penicillamine, but, if anything, slightly decreased the effect of 2,3-dimercaptopropanol. Sodium maleate, 25 mg/kg daily s.c. given on the sixth and seventh days after the administration of 100 μg Hg (as labelled $HgCl_2$), potentiated the effect of *d*-penicillamine (35.8 mg/kg I.M. twice a day), resulting in a urinary excretion of

4.2 μg Hg/day compared with 0.6 μg/day in the untreated controls or the 1.9 μg/day in the animals treated only with penicillamine.

Sodium maleate reduced the non-protein but not the protein-bound thiol groups in the kidney. Neither did it change the amount and the pattern of thiol compound excretion in the urine after penicillamine. Thus its effect on the mercury excretion cannot be explained by its action as a thiol reagent nor by any modification of the penicillamine excretion. Probably its effect was due to metabolic or permeability changes which facilitated the withdrawal of mercury by penicillamine. The binding site for sodium maleate in the kidney responsible for these changes was probably not a protein thiol group because with thiols maleate should form irreversible (covalent) bonds. The binding site was likely to be another reactive group with which maleate formed a reversible (ionic) bond. The affinity of sodium maleate for this reactive group might be higher than its affinity for penicillamine, but lower than that for dimercaptopropanol. Thus dimercaptopropanol given either simultaneously or even 3 hr after sodium maleate would be able to break this reversible bond and so abolish the change responsible for the increase in the mercury excretion.

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Effect of different dopa decarboxylase inhibitors on the hypotensive response to α-methyldopa in rats

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In order to explain the antihypertensive properties of L-α-methyl-3,4-dihydroxyphenylalanine (α-methyldopa), Day & Rand (1964) suggested that α-methylnoradrenaline formed from α-methyldopa may serve as a false transmitter in place of noradrenaline in peripheral sympathetic nerves. The theory implies that inhibition of the synthesis of false transmitters from α-methyldopa should abolish the hypotensive effect.

Carotid blood pressure was recorded in conscious Sprague-Dawley rats, 180–250 g, with renal hypertension (Henning, 1967). All drugs were injected intraperitoneally. After α-methyldopa (200 mg/kg) the maximal decrease in arterial blood pressure occurred after 3–6 hr (mean decrease after 3 hr: 46 mm Hg, S.E. of mean=5.2, n=8). Pretreatment with Ro 4-4602 (seryl-1,2,3-trihydroxybenzylhydrazine), a potent inhibitor of dopa decarboxylase in peripheral tissues and in brain, completely prevented the fall in blood pressure after α-methyldopa. The inhibitor was given 4×200 mg/kg at 2 hr interval, first dose 30 min before α-methyldopa. Mean decrease in blood pressure 3 hr after α-methyldopa plus Ro 4-4602 was 1 mm Hg (S.E. of mean=6.1, n=6), differing significantly ($P<0.025$) from the value after α-methyldopa only. In control experiments, Ro 4-4602 alone had a slight hypotensive effect 12–24 hr after the first dose. The accumulation of α-methyldopamine 3 and 6 hr after α-methyldopa (200 mg/kg) was inhibited completely in the heart and femoral muscle and to about 75% in the brain following the same pretreatment with Ro 4-4602.

Unlike Ro 4-4602, the decarboxylase inhibitor MK-485 (hydrazinomethyldopa) does not penetrate into the brain. Pretreatment with MK-485 (5×100 mg/kg at 2 hr interval, first dose 30 min before α-methyldopa) did not prevent the decrease in blood pressure