suggests that the widely accepted opinion that lactose is transported into the cells by the activity of a specific permease is not valid in all cases. Further drugs such as streptomycin, which inhibit permease synthesis, do not affect penetration of lactose. Lactose is, however, freely released by the cells, showing the membranes are permeable in both directions.

While experimental work is still in progress, it appears that current theories on membrane permeability and the action of drugs on the membrane need be carefully reconsidered. We believe that measurement of the water space available to single drugs provides a direct and reliable index of membrane permeability.

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Inhibition of oxidative phosphorylation by atractyloside in digitonin particles of mitochondria

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The effect of atractyloside on digitonin fragments of rat liver mitochondria was first studied by Vignais & Vignais (1961). They found that atractyloside inhibits the phosphate-adenosine triphosphate exchange reaction and 2, 4-dinitrophenol-stimulated adenosine triphosphatase but was inactive on phosphate uptake coupled with beta-hydroxybutyrate oxidation and on magnesium-stimulated adenosine triphosphatase. The ineffectiveness of atractyloside on the phosphate uptake could be explained by the high amount of adenosine diphosphate present in the incubation medium. In fact, an increase in the concentration of adenosine diphosphate competitively removed the effect of atractyloside on oxidative phosphorylation (Bruni, Contessa & Luciani, 1962).

To clarify this point, the effect of atractyloside on the digitonin particles of rat liver mitochondria was reinvestigated. It was found: (*a*) in agreement with Vignais & Vignais (1961) atractyloside inhibits the 2, 4-dinitrophenol-stimulated adenosine triphosphatase, the phosphate-adenosine triphosphate exchange reaction but it is ineffective on magnesium-stimulated adenosine triphosphatase; (*b*) using low concentrations of adenosine diphosphate, atractyloside fully inhibits the phosphorylation coupled with beta-hydroxybutyrate oxidation; (*c*) the binding of adenosine-diphosphate to digitonin submitochondrial particles is also sensitive to atractyloside.

These results show that submitochondrial particles prepared with digitonin react to atractyloside differently from phosphorylating particles prepared by sonic disinte-

gration. This latter preparation is completely insensitive to atractyloside (Low, Vallin & Alm, 1963).

Further investigations are needed to explain this difference.

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Inhibition by quercetin of magnesium-, sodium- and potassium-activated adenosine triphosphatase

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The flavonoid quercetin increases the strength of the heart beat, an effect which is not due to a local release of catecholamines or to a direct interaction with beta-receptors (see Santi, 1966). The potentiation of the effect of quercetin by decrease in calcium concentration and the observation (Carpenedo, Ferrari & Santi, 1968) that the drug promotes the release of bound calcium from isolated guinea-pig atria, suggests that quercetin inteferes with the mechanisms regulating the movement and utilization of calcium ions. We have studied the effect of quercetin on magnesium, potassium and sodium-activated adenosine triphosphatase.

The enzyme was prepared from beef heart (Matsui & Schwartz, 1966) and used after the first sodium deoxycholate treatment. At this level of purity the ouabain-sensitive portion of the freshly prepared enzyme was 50–55% of the total in the presence of 100 mM sodium and 20 mM potassium. The specific activity (ouabain-sensitive plus ouabain-insensitive) was 20–22 μ-moles adenosine triphosphate split/mg protein per hr at 37° C. Quercetin in concentrations of 0.001–0.2 mM was an active inhibitor of the enzyme. 50% inhibition was reached with 0.04 mM quercetin at level of 50 μg enzyme protein. Salient features of the inhibition were: (*a*) the effect was dependent on the ratio inhibitor/enzyme concentrations rather than on the concentration of the inhibitor in the incubation medium ; (*b*) unlike ouabain but like oligomycin, quercetin produced a significant inhibition of the magnesium-stimulated adenosine triphosphatase. Mitochondrial 2-4-dinitrophenol or magnesium-stimulated adenosine triphosphatase was also affected by quercetin ; (*c*) the inhibitory effect was more manifest at high (300–500 mM) sodium concentration or low (1 mM) potassium concentration.

These results support the possibility that quercetin influences the transport of ions across the cell membrane. Moreover, they suggest that quercetin inhibits the magnesium-, sodium- and potassium-activated adenosine triphosphatase by a different mechanism from that of cardiac glycosides.

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