

CARBOXYHAEMOGLOBIN INHIBITS INSULIN-STIMULATED GLUCOSE
UPTAKE IN PERFUSED RAT LIVER

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Uptake of glucose and synthesis of glycogen by the liver in vivo is well-documented as is the stimulatory action of insulin on both these processes. However, similar effects have been very difficult to obtain in vitro so that Stalmans (1976) has concluded that there may be a defect in isolated liver preparations. It does not appear that there is such a problem in liver perfused with undiluted rat blood where there is substantial uptake of exogenous glucose and synthesis of glycogen and where both activities are stimulated by insulin (Storer et al. 1981).

Since the effects of insulin are lost on dilution of blood with buffer (Storer et al. 1980) we have suggested that the disparity between these data and those obtained with other perfused liver preparations is in the use of undiluted blood with its high O₂ delivery compared with the more general use of lower haematocrits. However, these data do not necessarily indicate that O₂ supply is the limiting factor, because other blood or plasma constituents might be similarly diluted. Therefore, we have used blood equilibrated with carbon monoxide (CO) to modify the O₂ consumption of the perfused rat liver. CO combines with erythrocyte haemoglobin, forming a complex, carboxy-haemoglobin (COHb), which does not transport O₂. Other blood components are unmodified by this procedure.

Hepatic O₂ consumption was depressed by COHb in proportion to its blood concentration and, at a level of 40% of total haemoglobin, uptake of exogenous glucose and the stimulatory effects of insulin were abolished. These data strongly support the concept that effects of insulin on glucose metabolism by perfused rat liver depend upon O₂ availability. It would also appear that COHb found at significant levels in the blood of human smokers would impair insulin action. Such a notion provides a practical basis for the advice given to diabetics (where insulin is limited) not to smoke.

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