Transport and metabolism of propionate in isolated hepatocytes from sheep treated with glucagon

A Mohamed Ali, M Jois

School of Agriculture, La Trobe University, Bundoora, VIC 3083

We have shown that isolated perfused liver of sheep treated with glucagon shows increased uptake and conversion of propionate to glucose (1). In the present study we examined the transport and metabolism of propionate in isolated hepatocytes from control and glucagon treated sheep.

Ten cross-bred wethers (24-35 kg) were used. Glucagon (9.8 µg/min) or sterile saline was infused for 3 h into the jugular vein and then the caudal lobe of the liver was removed surgically under anaesthesia. The lobe was used to prepare hepatocytes by a two-step collagenase digestion method. Propionate transport into hepatocytes was initiated by adding appropriate amounts of [2-^{14}C] propionate to flasks containing hepatocytes suspended in the incubation medium previously described (1). After incubating for 30 seconds, 0.5 ml from each flask was placed onto 0.5 ml of 1-bromododecane layered on 50 µl of 30% perchloric acid in an Eppendorf tube and then rapidly centrifuged to separate cells from the medium. The radioactivity in the cell pellet was counted to determine the transport rate. Gluconeogenesis from propionate was determined in separate incubations. The gluconeogenic rate and the transport rate were also determined in the presence of 1.35 mM butyrate or 1 mM caproate.

Propionate transport was saturable (Figure), with a K_m of 0.24 ± 0.07 mM and a V_{max} of 6.7 ± 0.6 nmole/min/mg dry cells in the control group. For the glucagon group the respective values were 0.20 ± 0.04 mM and 6.2 ± 0.41 nmole/min/mg dry cells. Butyrate and caproate inhibited the transport rate by 64 and 50%, respectively. Glucagon stimulated gluconeogenesis from propionate by 22% (1.92 ± 0.08 vs 1.58 ± 0.12 nmoles glucose/min/mg dry cells; $P<0.05$). However, both butyrate and caproate completely abolished this stimulation.

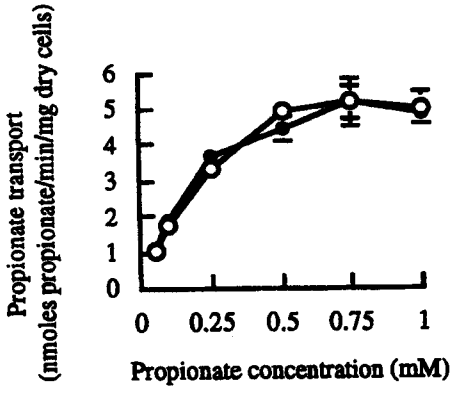

Figure. Transport of propionate into isolated hepatocytes prepared from sheep treated either with saline (o) or glucagon (•). Hepatocytes were incubated for 30 seconds in the presence of [2-^{14}C] propionate at the concentrations shown.

The results indicate that butyrate and caproate are potent inhibitors of propionate transport. The effect of glucagon on gluconeogenesis from propionate in hepatocytes is consistent with the effect we previously observed in isolated perfused caudal lobe of sheep liver. It is concluded therefore that glucagon regulates gluconeogenesis from propionate in sheep liver.

1. Mohamed Ali A, Jois M. Effects of administration of glucagon and epinephrine in vivo on the metabolism of propionate in subsequently isolated caudal lobe of sheep liver. Proc Nutr Soc Aust 1995;19:103.