Effect of diabetes mellitus and insulin on the regulation of the PepT 1 symporter in rat jejunum.


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This investigation focused on studying the effects of insulin-dependent diabetes mellitus and insulin treatment on absorption of glycylsarcosine (Gly-Sar) across the Sprague-Dawley rat jejunum, using in situ perfusion in a physiologic acidic microenvironment at pH 6.0. Rats were divided into five groups: normal controls in group I, normal colchicine-treated rats in group II, normal cytochalasin-treated rats in group III, streptozotocin-induced diabetic rats in group IV, and insulin-treated diabetic rats in group V. Histologic studies of the five different groups showed morphologic changes upon induction of diabetes and treatments with colchicine and cytochalasin and several variations in post-1 month diabetic rats treated with insulin. The rate of uptake of Gly-Sar was significantly reduced in the diabetic state. The comparison of colchicine-treated and cytochalasin-treated rats to the diabetic group suggests that an intact cytoskeleton and tight junctions may play a role in jejunal dipeptide absorption. In the diabetic and insulin-treated group, the dipeptide influx rate was significantly increased compared to that of the nontreated controls. The regulation of the PepT 1 symporter was further assessed by immunostaining and Western blot analyses in the normal, diabetic, and diabetic and insulin-treated groups. Our results showed that a downregulation of PepT 1 in the diabetics seemed to be due in part to the low systemic insulin levels, and not necessarily to hyperglycemia. In addition, the results suggest a probable role of systemic insulin binding at the vascular site of the jejunal epithelium, and the role that this hormone may be playing in the regulation and probably cellular trafficking of PepT1.

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