Tolbutamide Stimulates Ca^{2+} Influx in Islet Cells without Reducing K^+ Conductance

Dear Sir,

In a recent article published in this journal, Henquin [1] confirmed the observation reported elsewhere [2] that tolbutamide decreases K^+ outflow from rat pancreatic islets perfused with media containing little or no glucose. Henquin concluded that, by reducing K^+ permeability, tolbutamide depolarizes B-cells, causing in turn the gating of voltage-sensitive Ca^{2+} channels, facilitation of Ca^{2+} influx and stimulation of insulin release. Henquin, however, does not discuss his own finding that, in the presence of glucose 8.3 mmol/l, tolbutamide, instead of decreasing ^{86}Rb outflow, produces a transient increase in ^{86}Rb efflux and, nevertheless, rapidly augments insulin release. This finding is confirmed in Figure 1 which, in addition, indicates that the effect of tolbutamide upon insulin release, in the presence of glucose 8.3 mmol/l, coincides with a dramatic increase in ^{45}Ca fractional outflow rate. The latter effect, which was initiated prior to the increase in ^{86}Rb outflow, failed to occur in the absence of extracellular Ca^{2+} (data not shown) and, hence, probably corresponds to a process of ^{40}Ca - ^{45}Ca exchange [3]. This observation indicates that tolbutamide is able to stimulate both Ca^{2+} influx and insulin release in the absence of any decrease in K^+ conductance. It suggests that, under the present experimental conditions, the insulinotropic effect of the sulfonylurea may not be due to a gating of voltage-dependent Ca^{2+} channels. An alternative explanation would be that hypoglycemic sulfonylureas directly interfere with an ionophoretic modality of Ca^{2+} inwards transport in the B-cell, as proposed elsewhere [4, 5].

Yours sincerely,

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References

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Fig. 1. Effect of tolbutamide (100 µg/ml) upon ^{86}Rb and ^{45}Ca fractional outflow rate (F.O.R.) and insulin release from rat islets perfused in the presence of glucose 8.3 mmol/l. Mean values ($\pm$ SEM) for ^{86}Rb and ^{45}Ca F.O.R. refer to the same 6 individual experiments, insulin release being measured in only 4 of these 6 experiments