Abstract

In this dissertation, we focused on a comprehensive investigation of insulin production, storage and secretion by pancreatic β-cells. We successfully developed a new assay for the rapid and sensitive determination of insulin concentration in biological samples. This assay, based on the competition of the measured sample with a radioligand for the insulin receptor, helped us to determine the influence of several low molecular weight compounds, as well as peptides, on insulin secretion.

We found that arginine and ornithine have a dose-dependent stimulatory effect on glucose-stimulated insulin secretion from β-cells, but that dopamine inhibits insulin secretion. The effect of serotonin on insulin secretion was ambiguous.

We also studied the effects of the bone protein osteocalcin and its fragments on insulin secretion. We found that these peptides do not stimulate insulin secretion from β-cells, but that osteocalcin may have proliferative properties.

We also tested the effect of tryptophan and its metabolites and found that these compounds do not stimulate insulin secretion but that some of them may inhibit secretion at higher concentrations.

An important result of the study is the experimental confirmation of the presence of crystalline insulin in the secretory granules of β-cells. This is the first direct evidence that, under native conditions, insulin can be stored as microcrystals in cells.

Overall, we believe that the work was successful and achieved most of the stated objectives.