Supporting Information

Exploiting the Therapeutic Potential of 8-β-D-Glucopyranosylgenistein: Synthesis, Antidiabetic Activity and Molecular Interaction with IAPP and $A\beta_{1-42}$

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Antidiabetic Activity

Insulin secretion was assessed by C-peptide quantification (**Figure S1**) and circulating insulin evaluation during basal fasting and post-load intragastric tolerance test (**Figure S2**). β-cell sensitivity was likewise evaluated by the ratio of insulin secretion and corresponding circulating glycemia (**Figure S3**).

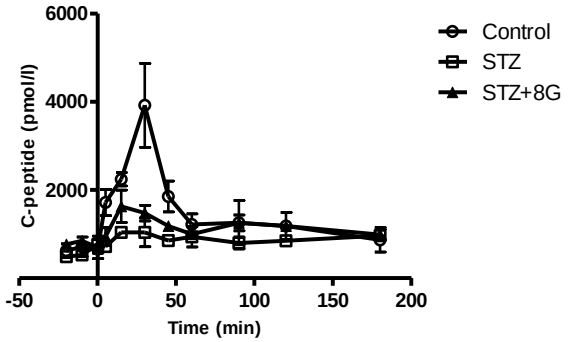

Figure S1. Dynamic curves for insulin secretion, assessed by C-peptide quantification, during basal fasting and post-load intragastric tolerance test (2 mg glucose/kg b.w.).

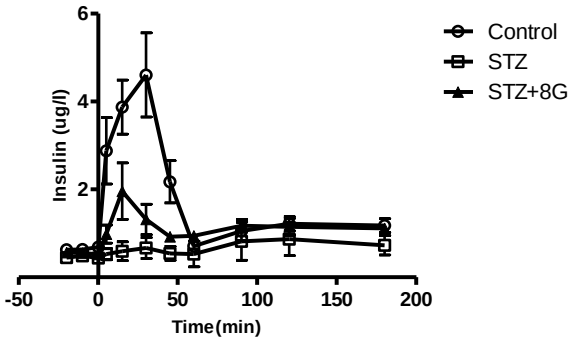

Figure S2.Dynamic curves for circulating insulin during basal fasting and post-load intragastric tolerance test (2 mg glucose/kg b.w.).

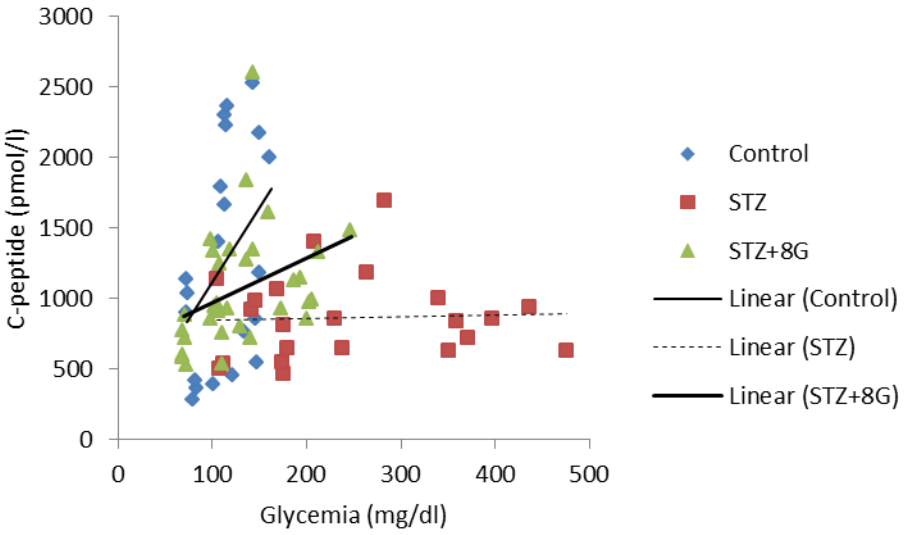

Figure S3. β-cell sensitivity during intragastric tolerance test (2 mg glucose/kg b.w.) for all groups, as assessed by the slope of the correlation of insulin secretion response to circulating glycemia.

ThT kinetics of IAPP fibrillization

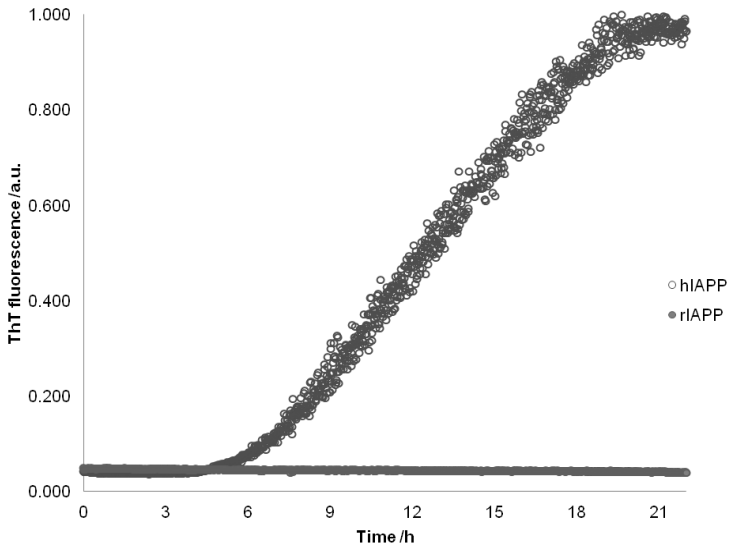

Figure S4. Kinetics of hIAPP fibril elongation, vs. that of rIAPP, at 25 ºC.

NMR Binding Studies with Islet Amyloid Peptide IAPP and $A\beta_{1-42}$ Oligomers

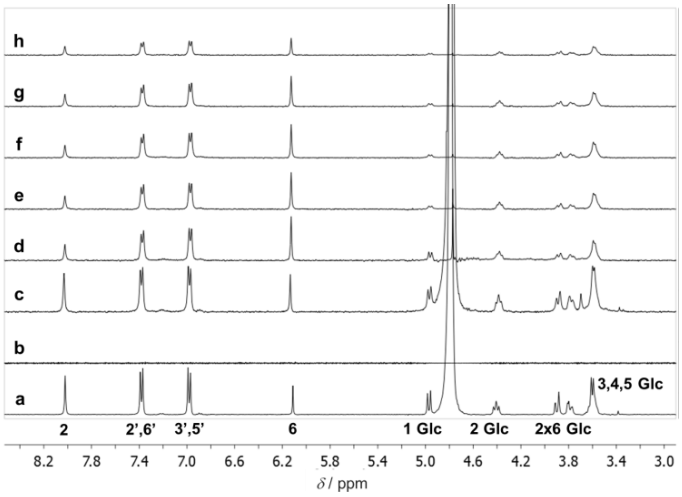

Figure S5. a) ^{1}H NMR spectrum of 2 mM 8-β-D-glucopyranosylgenistein; **b)** Blank STD-NMR spectrum of the same sample acquired with a saturation time of 2s; **c)** ^{1}H NMR spectrum of the mixture containing 80 µM Aβ1-42 and 2 mM 8-β-D-glucopyranosylgenistein; **d-h** STD-NMR spectra of the same mixture acquired with different saturation times. (**B**, 0.5 s; **C**, 1,2 s; **D**, 2,0 s; **E** 3,0 s; **F**, 5,0 s). Both samples were dissolved in deuterated PBS, pH 7.5, 25°C. The spectra were recorded at 400 MHz. The key resonances are highlighted in spectrum 4a in the bottom part.

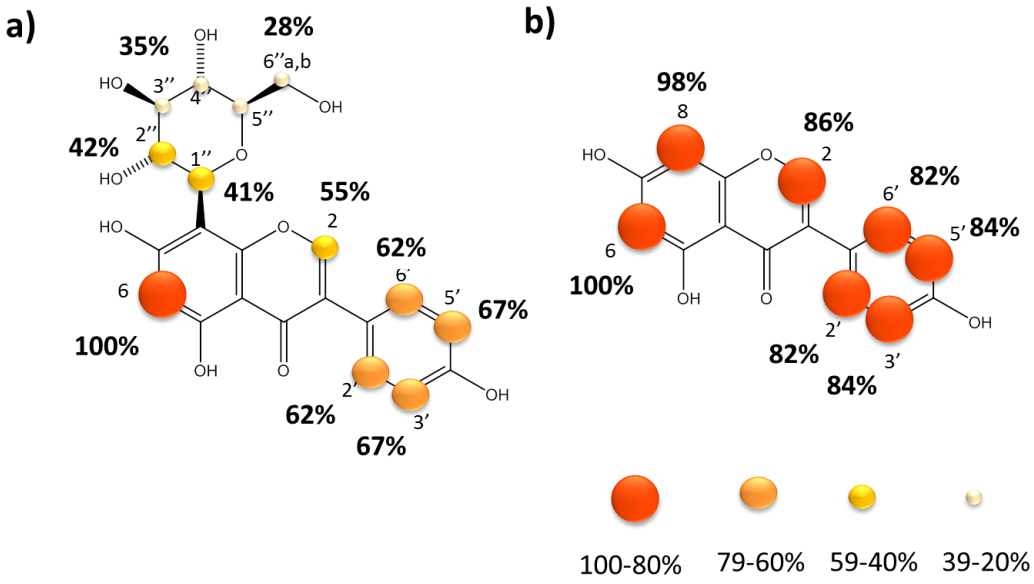

Figure S6. a) Epitope mapping of 8-β-D-glucopyranosylgenistein in the presence the of Aβ1-42 **b)** Epitope mapping of genistein in the presence the of Aβ1-42.