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An investigation into the possible beneficial effects of milk hydrolysates on insulin secretion and metabolic function

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In recent years, extensive research has provided evidence to suggest that bioactive peptides derived from food may exert beneficial effects on human health(1). Bioactive peptides have been identified within the amino acid sequences of bovine milk, which are released upon enzymatic hydrolysis using digestive enzymes(1). Moreover, milk derived bioactive peptides have previously been reported to generate beneficial effects on human cardiovascular, immune and nutrition systems(2). The objective of this study is to determine if milk derived hydrolysates have an effect on insulin secretion and glycemic function by firstly examining the possible insulinotropic properties on pancreatic β-cells *in vitro* and *in vivo* using an ob/ob mouse model. To investigate the insulinotropic effects of milk hydrolysates *in vitro*, BRIN-BD11 cells were treated with basal levels of glucose (1.1 mM) for 40 minutes prior to stimulating with 16.7 mM glucose and Hydrolysate A (1 mg/ml) for 20 minutes. A two-tiered model with human intestinal Caco-2 cells and pancreatic BRIN-BD11 cells were used in bioavailability studies. Hydrolysate A at a concentration of 1 mg/1 ml stimulated insulin secretion (5.5 ng insulin/mg protein) from BRIN-BD11 cells; the induction of insulin release was significantly different when compared to the control of unhydrolysed protein (0.265 ng insulin/mg protein), ($P<0.005$). Further analysis revealed that Hydrolysate A stimulated insulin release in a dose dependent manner (1.5 ng–10 ng insulin/mg protein at concentrations of 0.01–5 mg/ml). The bioavailability experiments demonstrated significant transport of the bioactive sample through the Caco-2 layer. After 4 hours, Hydrolysate A at 50 mg/ml + 100 mM glucose induced 4.6 ng insulin/mg protein from BRIN-BD11 cells as compared to 1.5 ng insulin/mg protein induced by the control of 100 mM glucose ($P<0.005$). The *in-vivo* effect of this hydrolysate is currently being assessed in an ob/ob model of diabetes. In conclusion, Hydrolysate A is a potent inducer of insulin secretion, which is bioavailable in a two-tiered co-culture model. Future work will be directed towards encompassing this bioactive into a functional food used to aid glycemic management.

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