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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<sup>(1)</sup>. Bioactive peptides have been identified within the amino acid sequences of bovine milk, which are released upon enzymatic hydrolysis using digestive enzymes<sup>(1)</sup>. Moreover, milk derived bioactive peptides have previously been reported to generate beneficial effects on human cardiovascular, immune and nutrition systems<sup>(2)</sup>. 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  $\beta$ -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.

1. FitzGerald RJ, Meisel H (2003) Milk protein hydrolysates and bioactive peptides 2.
2. Fox PF, McSweeney PLH (eds) Advanced Dairy Chemistry. Volume 1. Proteins. Part B, vol 1. 3rd edn. edn. Kluwer Academic/ Plenum Publishers, New-York, pp. 675–698.