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The role of coffee derivatives in the regulation of pancreatic beta cell function in Type 2 Diabetes

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Abstract
Coffee contains several components other than caffeine such as chlorogenic acids (CGAs), which are a family of polyphenols. Non-caffeinated coffee has been shown to reduce the risk of Type 2 diabetes, but it is unclear whether this effect is primarily due to a beneficial action on glucose regulation in peripheral tissues or whether it is partly mediated via a direct, functional modulation of insulin-secreting beta cells from the pancreas. This study aims to explore the specific role of coffee compounds derived from the polyphenolic family of CGAs (caffeic acid (CA) and ferulic acid (FA)) and their metabolites (dihydroferulic acid (diFA) and ferulic acid 4-O-sulphate (FA-4-OS)) in the regulation of beta cell survival and secretory function. To investigate this role, the cells were initially exposed to conditions of glucotoxicity (30mmol/l glucose), lipotoxicity (0.5mmol/l palmitate), glucolipotoxicity (30mmol/l glucose + 0.5mmol/l palmitate) and cytokine-induced cell toxicity (25U/ml IL1b + 500U/ml TNFα) for 20 and 48 h. INS1 beta cells were subsequently treated with or without 100nmol/l of the CGA compounds for 48 h followed by 20 h exposure to glucolipotoxicity to measure cellular ATP content and 3/7 caspase activity, respectively, as an indication of cell viability and apoptosis. Additionally, insulin release was assessed by radioimmunoassay following 1 h static incubations with or without CA, FA and metabolites. Data were analysed by One-Way ANOVA using GraphPad prism software (version 8). Glucotoxicity, lipotoxicity and glucotoxicity or glucolipotoxicity combined with cytokines significantly reduced INS1 cell viability compared to control at 20 and 48 h ($p < 0.001$ vs 11mmol/l glucose, $p < 0.05$; Glucotoxicity vs 11mmol/l glucose at 20 h, $n = 6$), whereas cytokines alone did not significantly affect cellular ATP content. Moreover, pre-treatment for 48 h with CGAs alone or in combination did not affect INS1 beta-cell viability under basal conditions ($n = 3$, $p > 0.2$). Additional exposure to glucolipotoxicity for 20 h significantly decreased beta cell viability and survival and was not alleviated by pre- or co-treatment with CGAs ($n = 3$, $p > 0.05$). However, insulin release in response to 1 h incubation with 20 mmol/l glucose + 10μmol/l forskolin (FSK) + 100μmol/l 3-isobutyl-1-methylxanthine (IBMX) was significantly higher from cells pre-treated with CA and FA combined compared to controls (7.64 + 2.89pg insulin/5,000 cells/h vs 2.17 + 0.35pg insulin/5,000 cells/h; $p < 0.01$ vs. 20mmol/l glucose + 10μmol/l FSK + 100μmol/l IBMX only, $n = 5$). The results suggest that CGA derivatives from coffee do not directly modulate INS1 beta cell viability and apoptosis whereas the compounds may play a role in the regulation of beta cell secretory function.

Conflict of Interest
There is no conflict of interest