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Effects of *Costus pictus* extract on GLP-1 secreting L-cell function

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Introduction: Glucagon-like peptide-1 (GLP-1) is a glucose-dependent insulinotropic hormone secreted by intestinal L-cells in response to nutrient ingestion. GLP-1 release is impaired in Type 2 Diabetes Mellitus (T2DM), thus, any compounds that might enhance endogenous GLP-1 release may have anti-diabetic therapeutic potential. *Costus pictus* D. Don (*C. Pictus*), known as the Insulin plant in southern India, is well known for its glucose lowering and insulin secretory effects [(1)]. It is used as a traditional Indian anti-diabetic medicine, although its mechanism of action is not fully understood [(2)]. As the potential actions of *C. Pictus* on gut L-cells have not been investigated, this study aimed to elucidate its effects using the murine GLP-1 secreting GLUTag L-cell model.

Methods: GLUTag cells were maintained in DMEM (1g/L D-Glucose) supplemented with 10% FBS, 50U/ml penicillin/streptomycin and 2mM L-Glutamine. *C. Pictus* dried leaf powder was extracted with ethanol using Soxhlet apparatus at 70^0C and residue was concentrated using rotary drum evaporator and reconstituted in ethanol to desired concentration. GLUTag cell viability was determined by MTT following treatment (24-48 h) of cells with different concentrations of *C. pictus* extract (CPE). Effects of culture (24-48 h) with CPE on L-cell specific gene expression were quantified by qPCR. CPE actions on intracellular calcium were determined in Fura-2AM loaded GLUTag cells. Acute effects of CPE on GLP-1 release were quantified using total GLP-1 ELISA (Millipore).

Results: Low concentrations (3.125 & 6.25 µg/ml) of CPE significantly ($p<0.01$) enhanced cell viability 1.25-1.29 fold following 24-48h culture, whereas higher concentrations (above 25 µg/ml) reduced cell viability ($p<0.001$). Following 24 & 48h culture with CPE (6.25µg/ml), glucagon gene expression was significantly downregulated (78% - 55%, $p<0.05$-0.01). Acutely, CPE raised intracellular calcium in GLUTag cells. Furthermore, CPE stimulated acute GLP-1 secretion up to 6.4 -16.3 fold (n=4) from GLUTag cells at both low (1.1 mM) and high (16.7 mM) glucose ($P<0.01$) concentrations.

Conclusion: Acute exposure of L-cells to CPE appears to enhance intracellular calcium and promote GLP-1 release, which may be beneficial in T2DM. Long term exposure of the cells to low concentrations also appears to enhance cell number, although down-regulation of glucagon gene expression occurs. Further studies are required to establish the mechanisms underlying CPE effects on L-cell function and GLP-1 secretion.

References:

1. Gireesh G et al. (2009) Journal of Ethnopharmacology, Volume 123, Issue 3, Pages 470-474
2. Hegde PK et al. (2014) Pharmacognosy review, Volume8, Issue 15, Pages 67-72