Acute Effect of chalcone P9 [(2E)-3-(1,3-Benzodioxol-5-yl)-1-(3',4'-dimethoxy-phenyl)-2-propen-1-one] in insulin secretion in rat pancreatic islets

Cazarolli, L.H.¹; Zanatta, A.P.²; Castro, A.J.G.²; Damazio, R.G.²; Mascarello, A.³; Chiaradia, L.D.³; Nunes, R.J.³; Yunes, R.A.³; Silva, F.R.M.B.²
¹Universidade Federal da Fronteira Sul, Campus Laranjeiras do Sul, PR; ²Departamento de Bioquímica, Universidade Federal de Santa Catarina, Florianópolis, SC, Brasil; ³Departamento de Química, Universidade Federal de Santa Catarina, Florianópolis, SC, Brasil.

Introduction: Natural or synthetic chalcones have been involved in carbohydrate metabolism, specially modulating glucose homeostasis. Objectives: The aim of this study was to investigate the effect of chalcone P9 on serum insulin secretion and calcium influx in isolated rat pancreatic islets. Methods: Fasted adult Wistar rats (Protocol CEUA-UFSC PP00414) were loaded with glucose (4 g/kg p.o.) plus glipizide (10 mg/kg) or chalcone P9 (10 mg/kg) by gavage. Insulin was measured at zero, 15, 30, 60 min after glucose overload by a rat insulin ELISA commercial kit. For the rat islet isolation and $^{45}$Ca$^{2+}$ influx experiments, the islets were isolated by collagenase digestion, then incubated for 10 min in KRb-HEPES buffer containing 0.1 microCi/ml $^{45}$Ca$^{2+}$ at 37°C, pH 7.4 and gassed with O$_2$:CO$_2$ (95:5% v/v) without or with chalcone P9 (0.1, 1, 10, 100, 1000 nM). Channel blockers or kinase inhibitors, glibenclamide (20 microM), diazoxide (250 microM), nifedipine (1microM), BAPTA-AM (50 microM), dantrolene (50 microM), estearoyl carnitine (1 microM) were added during the last 15 min before the treatment and maintained during the incubation. Cold buffer with lanthanum chloride (10 mM) was added to the samples at the end of incubation. Aliquots were taken from each sample for radioactivity measurement and were used for total protein quantification. Results and conclusions: Chalcone P9 significantly potentiated the insulin secretion induced by glucose overload. Chalcone P9 stimulated calcium influx and the involvement of ATP-sensitive potassium channels, L-type voltage-dependent calcium channels, the intracellular calcium and the PKC signaling pathways were evidenced in pancreatic islets. In conclusion, chalcone P9 potentiates insulin secretion in vivo and significantly stimulates calcium influx in rat pancreatic islets through closing K$^+$ATP channels, opening L-VDCC, altering intracellular calcium and PKC signaling pathways. These findings highlight chalcone P9 as a potential insulin secretagogue contributing to glucose homeostasis. Keywords: chalcone; rat pancreatic islets; insulin secretion. Supported by: CNPq and CAPES.