EFFECTS OF PORCINE GALANIN, GALANIN(1-15)NH₂ AND ITS NEW ANALOGUES ON GLUCOSE-INDUCED INSULIN SECRETION

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Porcine galanin (pGAL), its 15-amino-acid-residue fragment and five new analogues modified in positions 4, 6 or 14 were tested for their effects on glucose-induced insulin secretion from isolated rat pancreatic islets of Langerhans. In vitro insulin secretion was studied during static incubation. All peptides were tested at two concentrations: 100 nM and 1 µM. The insulin level in the presence of 10 mM of glucose was a reference for all experiments. Our studies have shown that porcine galanin and its fragment GAL(1-15)NH₂ at all concentrations tested inhibit glucose-induced insulin secretion. However, the modifications of the amino acid sequence of galanin caused changes in the interaction of GAL with its receptors, consequently yielding peptides that showed reverse activity as compared to pGAL or GAL(1-15)NH₂. Finally, we have found three analogues: [Cit⁴]GAL(1-15)NH₂, [Hse⁶]GAL(1-15)NH₂ and [Cle⁶]GAL(1-15)NH₂, which were able to stimulate glucose-induced insulin secretion and also antagonized inhibitory effect of pGAL. Other two galanin analogues: [D-Leu⁶]GAL(1-15)NH₂ and [des-Leu⁶]GAL(1-15)NH₂ showed a rather weak agonistic activity. Our observations suggest that positions: 4, 6 and 14 in the amino acid sequence of galanin may play an important role in the high-affinity binding of GAL to its receptors and biological action in perfused rat pancreas.

Key words: galanin, galanin analogues, insulin secretion, rat pancreatic islets