

P025 Conformational studies of an insulinotropic incretin (GIP) using spectroscopic and modelling techniques

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Type 2 diabetes is a metabolic disorder resulting from impaired insulin secretion & impaired insulin action. Due to loss of β -cell function, insufficient insulin is secreted to maintain normal glycaemia leading to a multiple complications. It is important to treat this condition appropriately and that necessitates the need for novel therapeutic agents. Glucose-dependent insulinotropic polypeptide (GIP) is a gastrointestinal hormone that enhances glucose stimulated insulin secretion by interacting with a hetero-trimeric G-protein coupled receptor (GPCR) located on pancreatic β -cell. Due to its glucose lowering and insulinotropic properties, GIP is considered as a potential target for treating type 2 diabetes. Our research focusses on structural studies of GIP and its analogues, to aid in understanding their biological role in insulin secretion. We are currently determining the solution conformation of GIP in various environments including water, TFE, micellar and bicellular media. We have shown that GIP adopts an α -helix, between the residues Ser¹¹-Ala²⁸, and is found to be the bioactive conformation of the peptide. Biological studies of N-terminal residues indicate that GIP(1-42)Ala⁶ could stimulate insulin secretion to a similar level of the parent GIP. These results could be useful in the design of successful peptide based drugs for treating type 2 diabetes.