

VVP808 IS A NOVEL AGENT THAT IMPROVES GLUCOSE TOLERANCE IN DIO MICE

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As the prevalence of diabetes mellitus continues to increase, there is an urgent need to discover new, effective treatment strategies to combat this disorder. In this study, we tested a novel agent, VVP808, which we previously demonstrated has insulin-sensitising properties (as measured by an increase in insulin-stimulated glucose uptake in 3T3-L1 adipocytes). A dose-ranging study was performed (10-100mg/kg/d) in C57BL/6J mice that had been fed a high-fat diet (45% of energy) for 12 weeks. VVP808 was administered by single daily oral gavage for a period of 16 days. Body weight, food intake and water intake were measured daily, whilst fasting blood glucose and plasma insulin levels were measured at the beginning and end of the study, with an intra-peritoneal glucose tolerance test (ipGTT) performed on day -1 and day 13. Administration of VVP808 to diet-induced obese (DIO) mice caused a strong dose-dependent improvement in glucose tolerance. There was a 34-42% reduction in the blood glucose area under the curve (AUC) at doses of 20mg/kg, 50mg/kg and 100mg/kg VVP808 ($p=0.02-0.005$). Administration of VVP808 resulted in a small but significant reduction in body weight in the 50mg/kg and 100mg/kg treated animals relative to vehicle ($p=0.01$ and 0.001 respectively). This decrease in body weight was associated with a reduction in food intake for the 100mg/kg treated animals only. Epididymal fat pad weight was significantly reduced in animals treated with 100mg/kg VVP808 ($p=0.01$). Furthermore, treatment with VVP808 for 16 days resulted in a highly significant dose-dependent reduction in fasting blood glucose levels relative to vehicle treated animals ($p=0.01-0.001$). In conclusion, our data showed that VVP808 acts in a dose-dependent manner to reduce fasting blood glucose levels and improve glucose tolerance. These data suggest that VVP808 is an interesting new agent with potential for development as a novel therapeutic for type 2 diabetes.