Physiogenex
THE METABOLIC DISEASES EXPERTS

Streptozotocin-induced diabetic rat model

✓ A widely used chemically-induced model of experimental diabetes to evaluate insulin analogues and bioactive compounds targeting diabetes

Key benefits

✓ ***Get a complete and rapid evaluation of your test item efficacy*** *on glycemic control, post-prandial glucose excursion and glucose tolerance in this chemically-induced rat model of experimental diabetes*

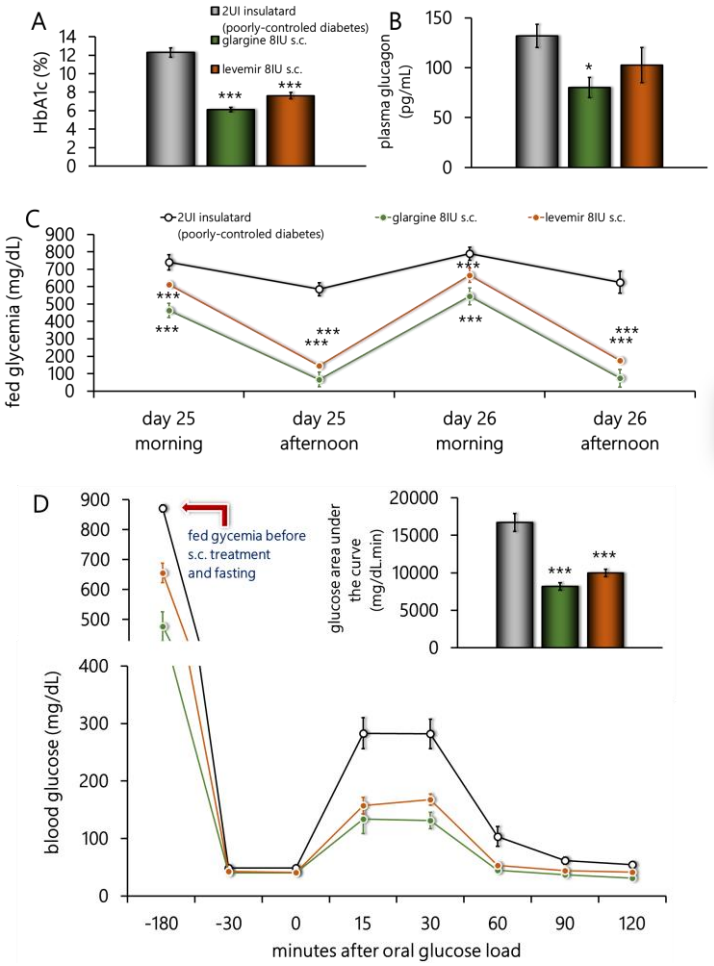
✓ ***Combine the streptozotocin rat model with our hyperinsulinemic euglycemic clamp technique using ^{3}H-glucose and conscious animals*** *to demonstrate and discriminate the mechanism by which your bioactive compound improves glucose and lipid homeostasis*

MODEL CHARACTERISTICS

- **Background strain:** Wistar rat, male, ~250g body weight
- **Streptozotocin (STZ) induction protocol:** STZ at 55mg/kg injected i.v., diabetic rats selection based on fed glycemia at 48 hours post-STZ, then 4 days recovery before acute or chronic treatment starts (group randomization based on overnight fasting glycemia)
- **Positive controls:** short- (lispro and glulisine) and long- (glargine and levemir) acting insulin analogues

DIFFERENTIATE ANALOGUES DURING CHRONIC TREATMENT

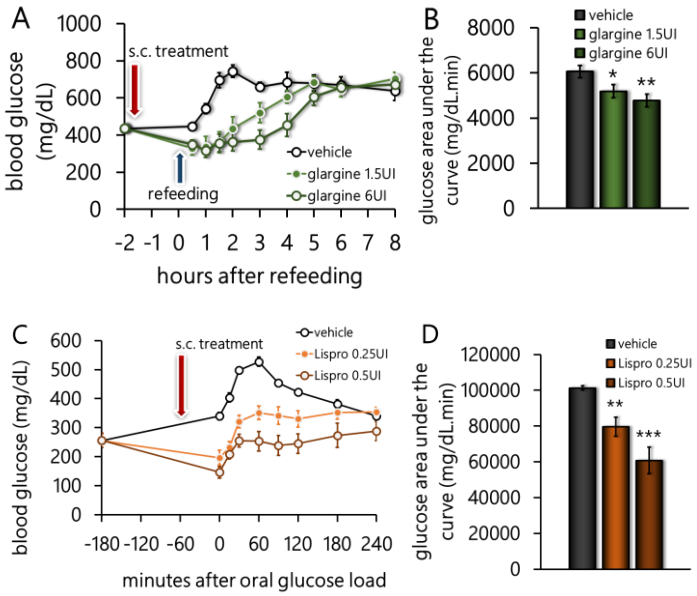
28-DAY TREATMENT WITH GLARGINE BETTER IMPROVES GLYCEMIC CONTROL THAN LEVEMIR



(A) HbA1c, (B) plasma glucagon, (C) fed glycemia follow-up and (D) oral glucose tolerance test in STZ rats treated in the morning with low dose 2UI insulatard (poorly-controlled diabetes), 8UI glargine or levemir for 28 days. *p<0.05 and ***p<0.01 vs. vehicle

ACUTE DOSE-DEPENDENT IMPACTS OF ANALOGUES

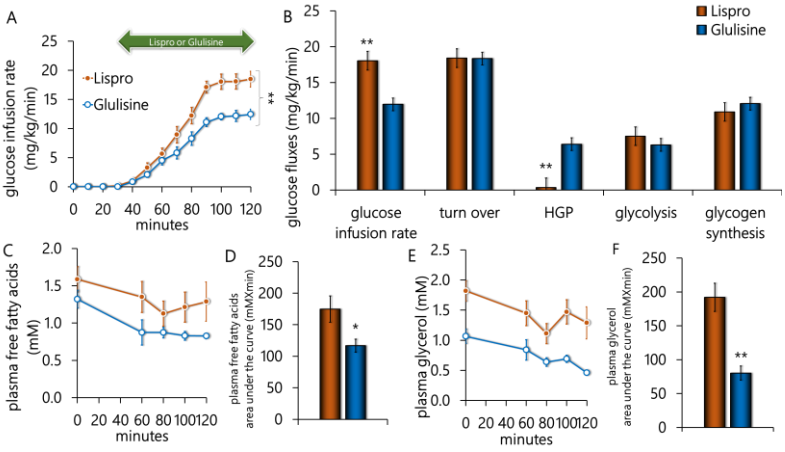
GLARGINE AND LISPRO DOSE-DEPENDENTLY REDUCE POST-PRANDIAL BLOOD GLUCOSE



(A) Blood glucose levels and (B) area under the curve during a refeeding experiment (free access to a 5% glucose rich diet), (C) blood glucose levels and (D) area under the curve during an oral glucose tolerance test in STZ rats treated with glargine or lispro. *p<0.05, **p<0.01 and ***p<0.01 vs. vehicle

DISCRIMINANT MECHANISMS USING HYPERINSULINEMIC CLAMP WITH ^{3}H-GLUCOSE

LISPRO BETTER REPRESSES HEPATIC GLUCOSE PRODUCTION, WHILE GLULISINE BETTER BLUNTS LIPOLYSIS



(A) Glucose infusion rates, (B) glucose fluxes, plasma free fatty acids (C) levels and (D) area under the curve, plasma glycerol (E) levels and (F) area under the curve in STZ rats infused with insulin analogs lispro or glulisine during a hyperinsulinemic euglycemic clamp. *p<0.05 and **p<0.01 Lispro vs. Glulisine

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