Physiogenex
THE METABOLIC DISEASES EXPERTS

Insulin resistant and dyslipidemic hamster

A diet-induced hamster model combining insulin resistance/diabetes and dyslipidemia

Key benefits

- ✓ Provides a noteworthy competitive advantage for your compound effects on both **insulin resistance/diabetes**, **dyslipidemia** and **hepatic steatosis**
- ✓ To select the best drug candidate in a very reproducible model with **lipoprotein metabolism** similar to humans
- ✓ To test the efficacy of novel drugs affecting both glucose and lipoprotein metabolism in a model validated with reference compounds

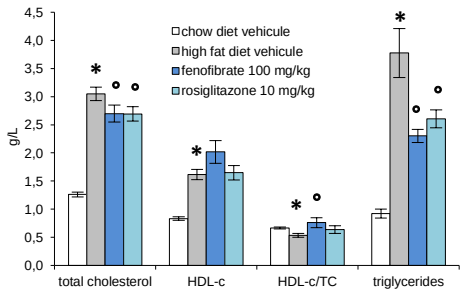
ANIMAL MODEL

- Background Strain: Golden Syrian Hamster
- Gender/Weight: male 90/110 g
- Diet: High fat diet + 10% fructose in drinking water
- Time on diet: 4 weeks
- Positive reference compounds:fenofibrate, rosiglitazone, sitagliptin

PHARMACOLOGICAL RELEVANCE

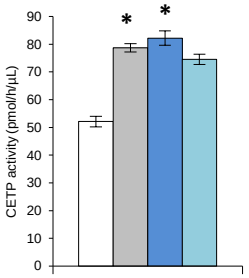
- A 4-week high fat diet induces hypercholesterolemia (140% increase), strong hypertriglyceridemia (300% increase), a 50% increase in CETP activity and a 20% decrease in HDL-c/total cholesterol ratio
- Fenofibrate lowers triglycerides and increases HDL-c/total cholesterol ratio (40% for both)
- Rosiglitazone lowers cholesterol (10%) and triglycerides (30%) plasma levels

Plasma total cholesterol, HDL-c, HDL-to-total cholesterol ratio and triglycerides



* p<0.05 *vs.* chow diet

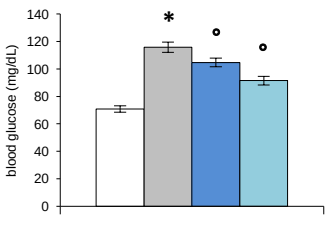
Plasma CETP activity



° p<0.05 *vs.* high fat diet

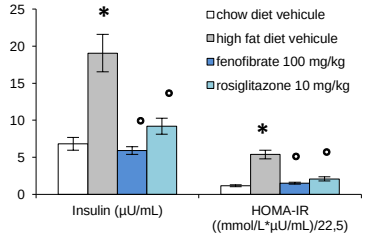
- A 4-week high fat diet increases fasting blood glucose by 60% and plasma insulin by 180%. HOMA-IR dramatically increases by 360%
- Both fenofibrate and rosiglitazone significantly decrease fasting blood glucose (10 and 20%), plasma insulin (69 and 52%) and HOMA-IR (72 and 61%)

Blood glucose levels after an overnight fasting



* p<0.05 *vs.* chow diet

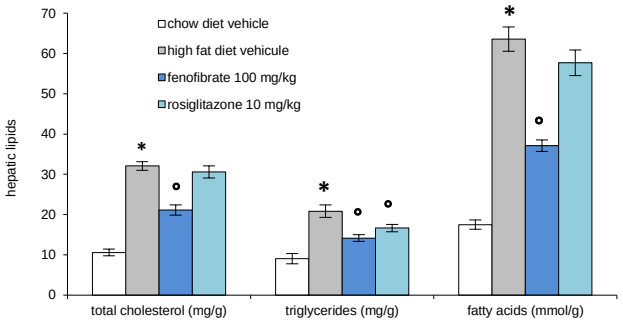
Plasma insulin and HOMA-IR after an overnight fasting



° p<0.05 *vs.* high fat diet vehicle

- A 4-week high fat diet induces a strong hepatic steatosis with a 203, 131 and 264% increase in total cholesterol triglycerides and fatty acids levels, respectively
- Rosiglitazone significantly decrease liver triglycerides by 20%. Fenofibrate decreases liver total cholesterol, triglycerides and fatty acids by 34, 32 and 42%, respectively

Liver total cholesterol, triglycerides and fatty acids levels

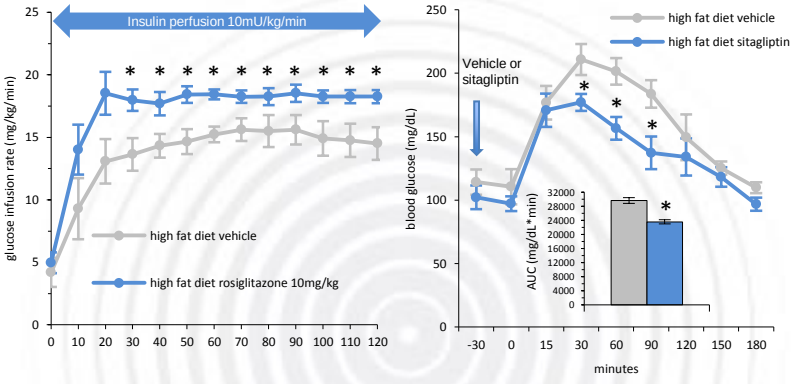


*p<0.05 *vs.* vehicle

- Rosiglitazone significantly improves insulin sensitivity, as measured by glucose infusion rate during euglycemic hyperinsulinemic clamp
- Sitagliptin administered acutely significantly improves glucose tolerance by 20%

Glucose infusion rate to maintain euglycemia during an euglycemic hyperinsulinemic clamp in conscious hamsters

Oral glucose tolerance test in conscious hamsters



*p<0.05 *vs.* chow

REFERENCES

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