Physiogenex
THE METABOLIC DISEASES EXPERTS

Hypercholesterolemic hamster

A nutritional hamster model dedicated to cholesterol & lipoprotein metabolism studies

Key benefits

- ✓ To select the best drug candidate in a very reproducible model with lipoprotein metabolism similar to humans (e.g.: high LDL-C levels and higher CETP activity)
- ✓ To test the efficacy of novel drugs in a model validated with reference compounds

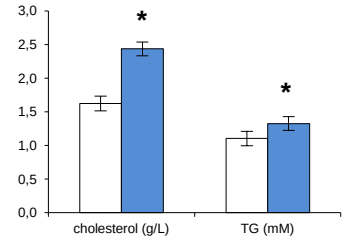
ANIMAL MODEL

- Background Strain: Golden Syrian hamster
- Gender/Weight: male 90/110 g
- Diet: chow+cholesterol 0.3%
- Time on diet: 4 weeks
- Positive reference compounds: fenofibrate, ezetimibe

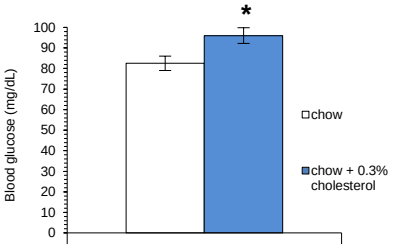
PATHOPHYSIOLOGICAL FEATURES

- Higher plasma cholesterol and triglycerides
- Higher blood glucose levels
- Higher VLDL-cholesterol and triglycerides
- Higher LDL-C levels
- Limited HDL-C increase

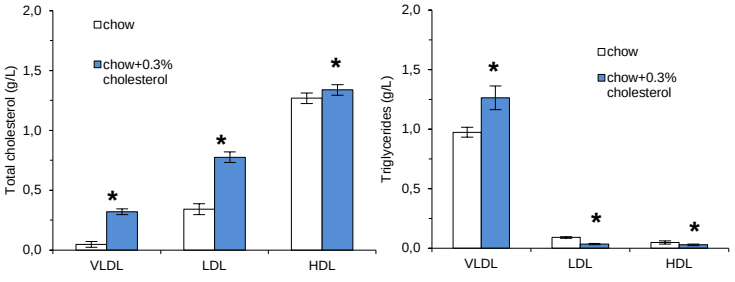
Plasma total cholesterol and triglycerides



Blood glucose



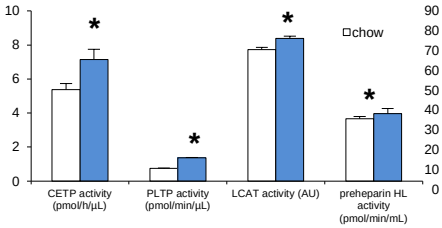
Total cholesterol and triglycérides in VLDL, LDL and HDL (HPLC analysis)



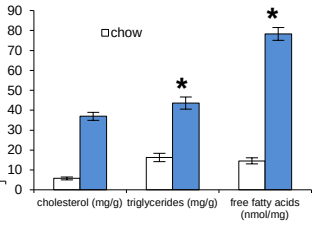
* p<0.05 vs. chow diet

- Higher CETP activity (33%)
- Higher PLTP activity (82%)
- Higher LCAT activity (8%)
- Hepatic steatosis/ higher liver cholesterol (535%), triglycerides (168%) and free fatty acids (437%)

Plasma CETP, PLTP, LCAT and pre-heparin HL



Liver cholesterol, triglycerides and free fatty acids

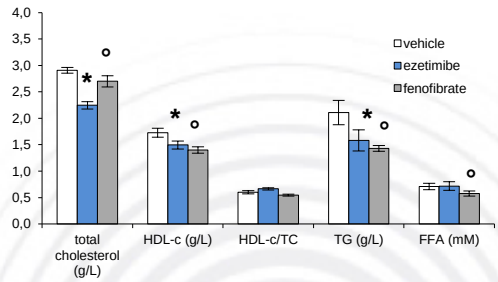


* p<0.05 vs. chow diet

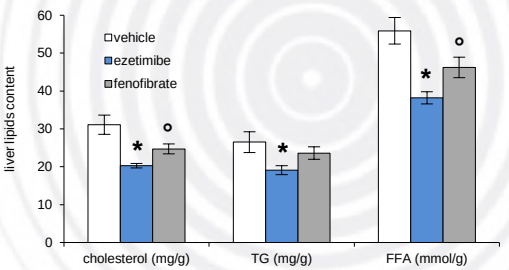
PHARMACOLOGICAL RELEVANCE

- 2-week treatment with fenofibrate 100mg/kg/day or ezetimibe 10mg/kg/day
- Fenofibrate lowers plasma cholesterol, triglycerides and free fatty acids
- Ezetimibe lowers plasma cholesterol and triglycerides
- Both ezetimibe and fenofibrate improve liver steatosis

Plasma total cholesterol, HDL-c, HDL-c to total cholesterol ratio (HDL-c/TC), triglycerides and free fatty acids



Hepatic total cholesterol, triglycerides and free fatty acids



*p<0.05 ezetimibe *vs.* vehicle °p<0.05 fenofibrate *vs.* vehicle

REFERENCES

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