Physiogenex
THE METABOLIC DISEASES EXPERTS

Diet Induced Obesity rat model

A nutritional rat model dedicated to obesity / insulin resistance studies

Key benefits

- ✓ To mimic gradual body weight gain, and especially visceral fat hypertrophy, as observed in western populations
- ✓ To select the best drug candidate in a reproducible model, suitable for screening
- ✓ To test the efficacy of compounds in a model with sensitivity to all reference compounds tested close to clinical setting

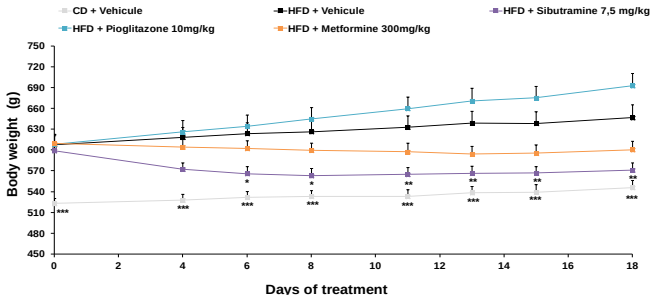
ANIMAL MODEL

- Background Strain: Sprague Dawley (SD) rat
- Gender/Weight: male 250/300g
- Diet: High fat - high carbohydrate
- Time on diet: ~8 weeks (depending on required severity)
- Positive reference compounds: sibutramine, pioglitazone, metformin

PATHOPHYSIOLOGICAL FEATURES

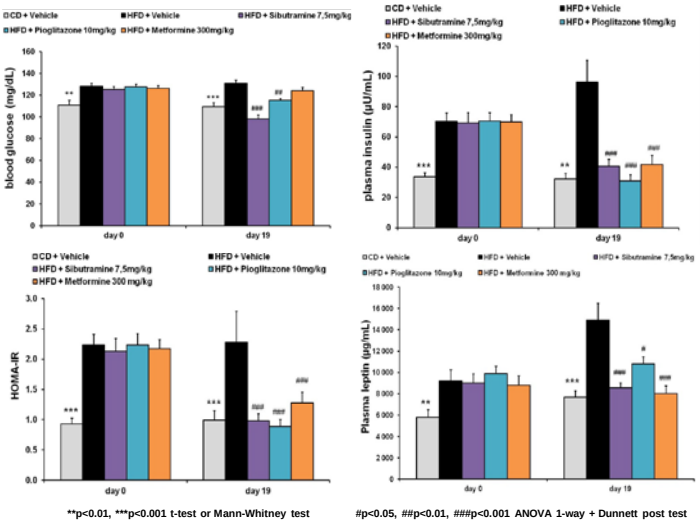
- Obesity (visceral and subcutaneous fat hypertrophy)
- Glucose intolerance
- Hyperinsulinemia
- Insulin resistance
- Hyperleptinemia
- Liver steatosis

Body weight follow-up after 8 weeks of HFD and during treatment



* p<0.05, **p<0.01, ***p<0.001 ANOVA 2-way + Bonferroni post test

Blood glucose, plasma insulin and leptin after 8 weeks of HFD and after 19 days of treatment (6 hours of fasting)



**p<0.01, ***p<0.001 t-test or Mann-Whitney test

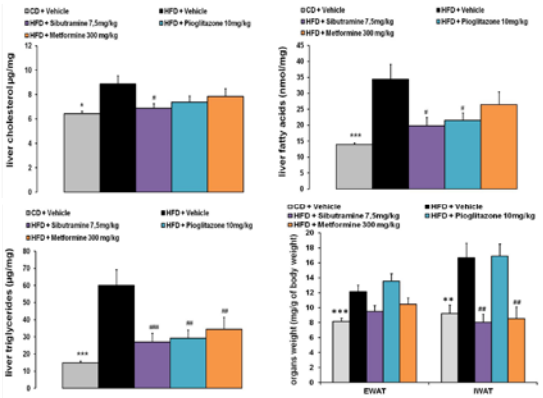
#p<0.05, ##p<0.01, ###p<0.001 ANOVA 1-way + Dunnett post test

PHARMACOLOGICAL RELEVANCE

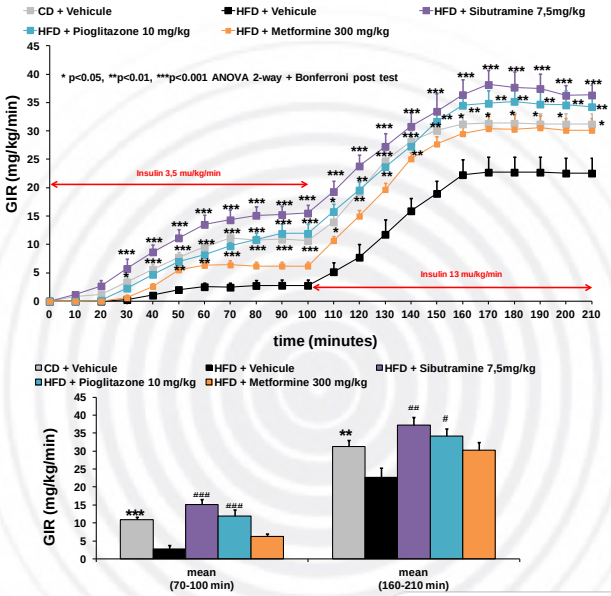
Reference compounds: sibutramin 7.5mg/kg, pioglitazone 10mg/kg, metformin 300mg/kg

- Treatments: chronic for 3 weeks.
- Sibutramin is the most efficient and improves the whole phenotype mainly *via* its satiating effect.
- Pioglitazone improves insulin resistance but enhances body wieght, as expected with a PPARγ agonist.
- Metformin mildly improves all parameters, as expected in a non hyperglycemic but insulin resistant model.

Liver lipids content and adipose tissues weight



Two steps hyperinsulinemic euglycemic clamp



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