

Fructose fed rats (FFR)

Model advantages:

The development of metabolic abnormalities induced by a fructose-enriched diet in rats is similar to what is observed in humans following an increased consumption of high-fructose corn sweetener (HFCS). Indeed, these HFCS is likely a decisive contributing factor to the development of obesity and the accompanying metabolic abnormalities observed in the insulin resistance syndrome.

Pathophysiological features:

Metabolic features:

- Hypertriglyceridemia
- Hypercholesterolemia
- Hyperinsulinemia
- Insulin resistance and exaggerated hyperglycaemic response to glucose overload
- Elevated urinary 8-isoprostanes (lipid peroxidation)

Cardiovascular features:

- Vascular endothelial dysfunction (aorta and superior mesenteric artery) (figure 1)

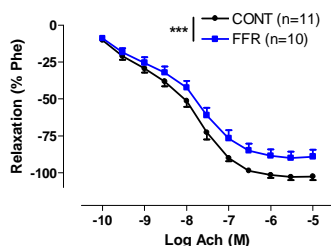


Figure 1: Comparison of endothelium-dependent relaxations obtained in *in vitro* experiments performed in aortic rings. (2-way ANOVA, ***P<0.001) (From Oudot et al. 2008).

- Exaggerated blood pressor response in vivo in conscious unrestrained animals (figure 2)

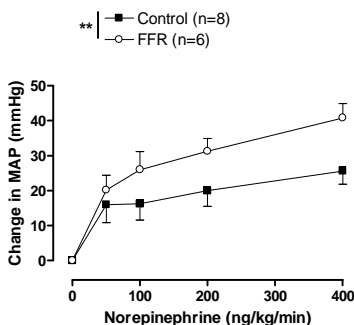


Figure 2: Concentration response curves to increasing doses of norepinephrine infusion (0 to 400 ng/kg/min) on mean arterial pressure (MAP) measured in vivo in conscious animals (control and fructose-fed rats (FFR)). (From Oudot et al. J Physiol Res 2008)

Summarized methodology:

Wistar rats are placed on a control or an isocaloric fructose-enriched diet containing 60% fructose and 5.2% lard for the following 9 weeks to allow the metabolic abnormalities to develop.

NB: Pelvipharm will gladly study the feasibility of modifying diet composition (fructose and lipid contents), way of administration and length of experimental period to meet its client's needs.

Related Pelvipharm bibliography:

- Oudot, A. et al. **J Sex Med** (2010) : 7(1)p1:79-88
- Oudot, A. et al. **Physiol Res** (2009) : 58(4):499-509
- Behr-Roussel, D. et al. **Eur Urol** (2008) : 53(6):1272-1281
- Behr-Roussel, D. et al. **Am J Hypertens** (2008) : 21(11): 1258-1263

Links to applicable experimental skills:

- Administration routes / regimen
- Plasma / urine / tissue collection
- In vivo experiments – conscious animals
 - * Telemetry
 - * Urine collection - Metabolic cages
 - * Tail cuff
- Organ bath studies (EFS / Pharmacological studies)
 - * Animal tissues
- Biochemistry (Plasma / Urine / Tissue)
 - * Spectrophotometric assays
 - * Protein expression and activity

- Histology

- * Histomorphology
- * Histomorphometry
- * Oxydative fuorescence

- Immunohistology / Confocal microscopy

- * Protein expression – immunohistochemistry / immunofluorescence
- * Confocal microscopy