

## Independent and Combined Effects of Menhaden Oil and High Fructose on Hepatic Lipid Metabolism

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### ABSTRACT

High-fat high-fructose foods have been attributed to the development of hypertriglyceridemia and hepatic lipotoxicity. Hypertriglyceridemia represents an important marker for cardiovascular disease (CVD) risk and may play critical roles in the development of insulin resistance. Furthermore, cardiovascular dysfunction has been associated with increased hepatic lipid deposition. The hypotriglyceridemic effect of omega-3 fatty acids (n-3fa), found in Menhaden oil, may prevent high-fat high-fructose induced fatty liver disease. The purpose of this study was to determine if a high-fat Menhaden oil diet provides a therapeutic strategy for reducing CVD risk by altering hepatic lipid deposition. For 14-weeks, 8-week old male C57BL/6J mice were randomly assigned to: low-fat diet (LFD; 10% kcal fat), high-fat diet plus a 20% fructose solution (HFD+HF; 60% kcal fat), Menhaden oil diet with 20% fructose solution (MOD+HF) or Menhaden oil diet alone (MOD). Plasma was analyzed for total cholesterol, insulin, triglyceride, and glucose concentrations. To characterize hepatic lipotoxicity, tissue was analyzed for total lipid, triglyceride and cholesterol levels. Following the 14-weeks, the HFD+HF, MOD and MOD+HF diets (Table 1) developed obesity and diabetes. The addition of HF to the MOD diet resulted in significantly ( $P < 0.05$ ) elevated plasma cholesterol and triglyceride levels. The MOD+HF displayed a significantly ( $P < 0.05$ ) greater hepatic mass and hepatic cholesterol levels than the MOD and LFD groups. A high-fat Menhaden oil diet rich in n-3fa with or without HF does not prevent the imbalance in hepatic lipid metabolism normally found with obesity and type 2 diabetes.

**Table 1.** Whole body and hepatic metabolic characteristics following the 14-week diet intervention.

Variables	LFD (n=8)	HFD+HF (n=8)	MOD (n=6)	MOD+HF (n=6)
Body mass (g)	27.5 ± 0.6	44.0 ± 1.5*	42.8 ± 1.2*	44.5 ± 1.9*
Liver mass (g)	1.2 ± 0.1	2.1 ± 0.2*	1.8 ± 0.2*	2.5 ± 0.3*‡
Triglyceride (mg/dL)	103.8 ± 5.9	142.3 ± 15.0*	134.2 ± 9.7	142.8 ± 9.4*
Cholesterol (mg/dL)	131.3 ± 6.4	193.2 ± 10.9*	146.4 ± 12.3†	228.7 ± 12.8*‡‡
Glucose (mg/dL)	158.2 ± 24.3	241.9 ± 32.2*	249.7 ± 10.1*	281.2 ± 15.2*
Insulin (ng/mL)	0.6 ± 0.1	2.1 ± 0.9*	2.0 ± 0.6*	2.5 ± 0.7*
HOMA-IR	5.5 ± 1.2	32.1 ± 7.5*	28.6 ± 8.8*	38.9 ± 10.5*
Liver Tg (µg/mg tissue)	10.5 ± 1.6	69.4 ± 5.7*	24.1 ± 3.6†	39.2 ± 10.4*†
Liver Chol (µg/mg tissue)	10.4 ± 0.9	8.0 ± 0.6*	10.2 ± 0.7	12.9 ± 0.8*‡‡

Note. Data are presented as mean ± SEM. Low-fat diet (LFD); high-fat diet and 20% fructose solution (HFD+HF); high-fat Menhaden oil diet (MOD); MOD and 20% fructose solution (MOD+HF). \*Significantly ( $P < 0.05$ ) different than LFD; †significantly ( $P < 0.05$ ) different than HFD+HF; ‡significantly ( $P < 0.05$ ) different than MOD.