

## **EFFECTS OF SYNTHETIC AND NATURAL PPAR LIGANDS ON THE CHOLESTERYL ESTER TRANSFER PROTEIN (CETP) EXPRESSION AND ACTIVITY IN TRANSGENIC MICE.**

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CETP reduces plasma HDL-cholesterol and increases atherosclerosis risk. Fibrates and fish oil are used to treat hypertriglyceridemia and their actions are mediated by the activation of the nuclear receptors PPAR $\alpha$ . n-3 and n-6 polyunsaturated fatty acid found in fish and corn oils, respectively, are natural ligands whereas fibrates are synthetic ligands of PPAR $\alpha$ . The aim of this work was to evaluate the potential effects of these oils and fibrates on the expression of CETP. Therefore, CETP transgenic mice were treated during 2 weeks with fish oil (FO), corn oil (CO), gemfibrozil (GEM), fenofibrate (FENO), bezafibrate (BEZA), ciprofibrate (CIPRO) and saline (control). FO diminished plasma free fatty acids when compared to controls and reduced total cholesterol when compared to CO group. Both oil treatments had no effect on the plasma CETP activity. GEM, FENO and BEZA increased cholesterol and GEM, FENO and CIPRO increased glucose plasma levels. FENO also reduced triglyceride levels. Three out of the four fibrates (GEM, FENO and CIPRO) induced elevation in plasma CETP activity and liver mRNA expression when compared to controls. In conclusion, natural ligands of PPAR $\alpha$  did not alter whereas three fibrates increased CETP activity and expression. These results may explain why fibrates do not increase HDL-cholesterol.

Key words: fibrates, fish oil, PPAR.

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