Supplementary Material

Oral Glucose Tolerance Test (OGTT): After a 12-hour fast, subjects were given 75 grams oral glucose solution. Plasma glucose, insulin levels, C-peptides and free fatty acids were obtained from blood samples drawn at –15, 0, 30, 60, 90, 120 and 180 minutes from intravenous line after the oral glucose load.

Frequently Sampled Intravenous Glucose Tolerance Test (FSIGT): Insulin resistance was determined by the Insulin Sensitivity Index (S_I) using minimal model equations with data from the insulin-modified frequently sampled intravenous glucose tolerance test (IM-FSIGT) (MinMOD Millenium v6.01, MinMOD Inc., Los Angeles, CA). The IM-FSIGT was performed at 8AM after a 12 hour fast. At time 0 glucose (0.3g/kg) was injected over 1 minute. At 20 minutes an intravenous bolus of insulin (0.03mU/kg) was given. Glucose and insulin concentrations were determined at -10, -1, 0, 1, 2, 3, 4, 5, 6, 7, 8, 10, 12, 14, 16, 19, 22, 23, 24, 25, 27, 30, 40, 50, 60, 70, 80, 90, 100, 120, 150, 180 min.

Body Mass Index (BMI): Weight (kg) and height (m) were recorded with empty bowel and bladder. BMI was calculated by the formula: BMI = weight (kg)/ height $(m)^2$.

***Waist/Hip Ratio*:** A trained investigator measured waist/hip ratio at the start and end of the 48 weeks of treatment.

Dual Energy X-ray Absorptiometry (DEXA): DEXA was used to estimate total body fat. Whole body composition measurement were made, using a Hologic QDR 4500A DEXA in the array beam whole body mode with software version 8.26a:3. Mass (in grams) of total body and regional fat content were determined.

Computerized Tomography (CT) of the Abdomen: 10mm CT slices were obtained at the level of lumbar spine vertebrae 2-3 and 4-5. The images were analyzed by MEDX image analysis software (Sensor System, Inc, Sterling, VA) and the total abdominal adipose tissue, visceral adipose tissue and subcutaneous adipose tissue volumes were calculated.

Magnetic resonance imaging (MRI*)* of the liver: MRI was done to evaluate liver size and estimate liver fat content. MRI scans were done as previously described (*promrat et al*). Axial in-phase and out-of-phase breath-hold gradient echo scans of the liver were obtained with previously described parameters (*promrat et al*). The analysis to quantify fat in the liver and measurements of liver volume was done using the MEDex software analysis package (Sensor Systems, Inc., Sterling, VA) run on a Linux platform. The modified Dixon method was used to measure hepatic fat fraction. Region of interest (ROIs) were placed in liver on the in-phase scans to include maximum liver parenchyma without contamination with blood vessels or motion artifacts. The MEDex software package then transposed these same ROIs onto the out-of-phase images and calculated the hepatic fat fraction (FF) based upon the following formula: FF = (Signal in-phase-signal out-of-phase)/(2 X Signal in-phase).