Bezafibrate Improves Insulin Sensitivity and Metabolic Flexibility in STZ-Induced Diabetic Mice.

Bezafibrate (BEZ), a pan activator of peroxisome proliferator-activated receptors (PPARs), has been generally used to treat hyperlipidemia for decades. Clinical trials with type 2 diabetes patients indicated that BEZ also has beneficial effects on glucose metabolism, although the underlying mechanisms of these effects remain elusive. Even less is known about a potential role for BEZ in treating type 1 diabetes. Here we show that BEZ markedly improves hyperglycemia and glucose and insulin tolerance in mice with streptozotocin (STZ)-induced diabetes, an insulin-deficient mouse model of type 1 diabetes. BEZ treatment of STZ mice significantly suppressed the hepatic expression of genes that are annotated in inflammatory processes, whereas the expression of PPAR and insulin target gene transcripts was increased. Furthermore, BEZ-treated mice also exhibited improved metabolic flexibility as well as an enhanced mitochondrial mass and function in the liver. Finally,
we show that the number of pancreatic islets and the area of insulin-positive cells tended to be higher in BEZ-treated mice. Our data suggest that BEZ may improve impaired glucose metabolism by augmenting hepatic mitochondrial performance, suppressing hepatic inflammatory pathways, and improving insulin sensitivity and metabolic flexibility. Thus, BEZ treatment might also be useful for patients with impaired glucose tolerance or diabetes.