**Summary:**
PEPCK is an enzyme critical in the process of gluconeogenesis whose inhibition could be used to treat hyperglycemia and diabetes.

**Applications:**
Inhibition of Phosphoenolpyruvate carboxykinase (PEPCK) is a promising new therapeutic approach to treating diabetes and preventing diabetic complications such as circulatory problems, heart disease, and blindness. The novel compounds are highly selective for PEPCK.

The novel compounds can be used to treat both acute hyperglycemia and secondary long-term complications from hyperglycemia. The invention covers both composition of matter and a scaffold to allow for chemical substitutions that provide functionalities to participate in as many interactions with PEPCK as possible.

**Overview:**
PEPCK catalyzes the first committed step in hepatic gluconeogenesis and is a key regulator of blood glucose homeostasis. Overexpression of this enzyme results in pre-diabetes and diabetes. PEPCK expression is stimulated by glucagon, glucocorticoids, retinoic acid and adenosine 3', 5'-monophosphate (cAMP) and is inhibited predominantly by insulin. Insulin levels of diabetic patients are insufficient to adequately inhibit PEPCK. Inhibition of PEPCK with siRNA led to complete elimination of hyperglycemia in a diabetic mouse model.

Current therapies for diabetic hyperglycemia are ineffective and wrought with adverse side effects due to unselective inhibition of various biological processes. KU’s portfolio of PEPCK inhibitors selectively and potently inhibit the enzyme to effectively eliminate production of glucose by the liver. This information was used to design new therapeutic compounds.

**Patents:**
US 2013/0109031

**Additional Web Content:**
Contact the inventor, [Gerald Carlson](mailto:gerald.carlson@ku.edu).