

## **Chlorogenic Acid and Synthetic Chlorogenic Acid Derivatives: Novel Inhibitors of Hepatic Glucose-6-phosphate Translocase**

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### **Abstract:**

The enzyme system glucose-6-phosphatase (EC 3.1.3.9) plays a major role in the homeostatic regulation of blood glucose. It is responsible for the formation of endogenous glucose originating from gluconeogenesis and glycogenolysis. Recently, chlorogenic acid was identified as a specific inhibitor of the glucose-6-phosphate translocase component (G1-6-P translocase) of this enzyme system in microsomes of rat liver. Glucose-6-phosphate hydrolysis was determined in the presence of chlorogenic acid or of new synthesized derivatives in intact rat liver microsomes in order to assess the inhibitory potency of the compounds on the translocase component. Variation in the 3-position of chlorogenic acid had only poor effects on inhibitory potency. Introduction of lipophilic side chain in the 1-position led to 100-fold more potent inhibitors. Functional assays on isolated perfused rat liver with compound 29i, a representative of the more potent derivatives, showed a dose-dependent inhibition of gluconeogenesis and glycogenolysis, suggesting glucose-6-phosphatase as the locus of interference of the compound for inhibition of hepatic glucose production also in the isolated organ model. G1-6-P translocase inhibitors may be useful for the reduction of inappropriately high rates of hepatic glucose output often found in non-insulin-dependent diabetes.

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