

**Benfotiamine Slowing the Process of Cellular Aging  
Benfotiamine Inhibits Intracellular Formation of  
Advanced Glycation End Products in vivo**

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**Abstract**

We have demonstrated previously that intracellular formation of the advanced glycation end product (AGE) N-epsilon-(carboxymethyl)-lysine (CML) inversely correlates with diabetic vascular complications independently from glycemia (Diabetologia 42, 603, 1999). Here, we studied the effect of benfotiamine, a lipid-soluble thiamine derivative with known AGE-inhibiting properties in-vitro on the intracellular formation of (CML) and methylglyoxal-derived AGE in red blood cells. Blood was collected from 6 Type 1 diabetic patients (2 m, 4 f, age  $31.8 \pm 5.5$  years; diabetes duration  $15.3 \pm 7.0$  years) before and after treatment with 600 mg/day benfotiamine for 28 days. In addition to HbA1c (HULK), CML and methylglyoxal were measured using specific antibodies and a quantitative dot blot technique. While treatment with benfotiamine did not affect HbA1c levels (at entry:  $7.18 \pm 0.86\%$ ; at conclusion  $6.88 \pm 0.88\%$ ; p not significant), levels of CML decreased by 40 % ( $737 \pm 51$  arbitrary unit/mg protein (AU) vs.  $470 \pm 86$  AU;  $p < 0.001$ ). The levels of intracellular methylglyoxal-derived AGE were reduced by almost 70% ( $1628 \pm 1136$  AU vs.  $500 \pm 343$  AU;  $p < 0.01$ ). The data indicate that thiamine derivatives are effective inhibitors of both intracellular glycoxidation and AGE formation.

**INTRODUCTION**

Intracellular formation of the advanced glycation end product (AGE) N-(carboxymethyl)lysine (CML) inversely correlates with diabetic vascular complications independently from glycemia. (1) Intracellular CML is generated by the oxidation of Amadori products or, alternatively, by lipid peroxidation (2,3). The dicarbonylmethylglyoxal is formed by non-oxidative fragmentation of glycolysis-derived triosephosphates and is the most important intracellular AGE (4,5).

Thiamine is a potent AGE-inhibitor in-vitro (6), and benfotiamine, the lipid-soluble pro-drug of thiamine was

shown to reduce CML and other AGE in target tissues of diabetic complications in-vivo (7). We studied the effect of benfotiamine, a lipid-soluble thiamine derivative with known AGE-inhibiting properties in-vitro on the intracellular formation of (CML) and methylglyoxal-derived AGE in red blood cells of patients with type 1 diabetes.

#### METHODS

Study group: six patients (2 males, 4 females), age  $31.8 \pm 5.5$  years; diabetes duration  $15.3 \pm 7.0$  years. Treatment with 600 mg/day benfotiamine for 28 days after informed consent and approval by the local ethics committee. Venous EDTA-blood (3 ml) drawn before and at the end of the study, samples lysed and centrifuged, adjusted to identical hemoglobin concentrations. Quantitative immunoblotting carried out essentially as described before (1). Statistical analysis was performed using the alternate Welsh t test.

#### CONCLUSION

Thiamine derivatives, in particular the lipid-soluble pro-drug benfotiamine, are effective inhibitor of intracellular formation of AGE and CML.

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