

1: [Diabetes](#). 2004 Jul;53(7):1813-23.



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Erratum in:

Diabetes. 2006 Mar;55(3):862. Thorpe, Susan M [corrected to Thorpe, Susan R].

**Advanced glycation end product interventions reduce diabetes-accelerated atherosclerosis.**

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Advanced glycation end product (AGE) formation may contribute to the progression of atherosclerosis, particularly in diabetes. The present study explored atherosclerosis in streptozotocin-induced diabetic apolipoprotein E-deficient (apoE<sup>-/-</sup>) mice that were randomized (n = 20) to receive for 20 weeks no treatment, the AGE cross-link breaker ALT-711, or the inhibitor of AGE formation aminoguanidine (AG). A sixfold increase in plaque area with diabetes was attenuated by 30% with ALT-711 and by 40% in AG-treated mice. Regional distribution of plaque demonstrated no reduction in plaque area or complexity within the aortic arch with treatment, in contrast to the thoracic and abdominal aortas, where significant attenuation was seen. Diabetes-associated accumulation of AGEs in aortas and plasma and decreases in skin collagen solubility were ameliorated by both treatments, in addition to reductions in the vascular receptor for AGE. Collagen-associated reductions in the AGEs carboxymethyllysine and carboxyethyllysine were identified with both treatments. Diabetes was also accompanied by aortic accumulation of total collagen, specifically collagens I, III, and IV, as well as increases in the profibrotic cytokines transforming growth factor-beta and connective tissue growth factor and in cellular alpha-smooth muscle actin. Attenuation of these changes was seen in both treated diabetic groups. ALT-711 and AG demonstrated the ability to reduce vascular AGE accumulation in addition to attenuating atherosclerosis in these diabetic mice.

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