

Renal accumulation and clearance of advanced glycation end-products in type 2 diabetic nephropathy: effect of angiotensin-converting enzyme and vasopectidase inhibition.

- [Wihler C](#),
- [Schafer S](#),
- [Schmid K](#),
- [Deemer EK](#),
- [Munch G](#),
- [Bleich M](#),
- [Busch AE](#),
- [Dingermann T](#),
- [Somoza V](#),
- [Baynes JW](#),
- [Huber J](#).

Therapeutic Department Cardiovascular, Aventis Pharma Deutschland GmbH, 65926 Frankfurt am Main, Germany.

AIMS/HYPOTHESIS: Renal accumulation of AGEs may contribute to the progression of diabetic nephropathy. We evaluated the effect of ramipril (a pure ACE inhibitor) and AVE7688 (a dual inhibitor of ACE and neutral endopeptidase) on renal accumulation of the advanced glycation end-product (AGE) 3-deoxyglucosone-imidazolone, carboxymethyllysine (CML) and pentosidine, and on clearance of CML in type 2 diabetes. **METHODS:** Male Zucker diabetic fatty rats (ZDF, Gmi-fa/fa) rats were treated from age 10 to 37 weeks with ramipril (1 mg.kg(-1).day(-1)), AVE7688 (45 mg.kg(-1).day(-1)) or without drug. Ramipril and AVE7688 reduced albuminuria by 30 and 90%, respectively. **RESULTS:** ZDF rats showed increased renal accumulation of the AGE subtypes 3-deoxyglucosone-imidazolone, pentosidine and CML by about 40, 55 and 55%, respectively compared with heterozygous, non-diabetic control animals at the age of 37 weeks. AVE7688 but not ramipril attenuated the renal accumulation of 3-deoxyglucosone-imidazolone, pentosidine and CML and improved CML clearance in ZDF rats. During glycation reactions in vitro, AVE7688 also demonstrated potent chelating activity and inhibited metal-catalysed formation of pentosidine and CML. **CONCLUSIONS/INTERPRETATION:** Improved AGE clearance and direct inhibition of AGE formation by chelation may contribute to reduced accumulation of renal AGEs and to the nephroprotective effects of vasopectidase inhibition in type 2 diabetes.

PMID: 16010524 [PubMed - indexed for MEDLINE]