

Telmisartan inhibits AGE-induced C-reactive protein production through downregulation of the receptor for AGE via peroxisome proliferator-activated receptor-gamma activation.

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AIMS/HYPOTHESIS: C-reactive protein (CRP), an acute-phase reactant produced mainly by the liver, is elevated in diabetes, thus contributing to the development and progression of atherosclerosis. However, the molecular mechanism underlying the elevation of CRP in diabetes is not fully understood. Since a crosstalk between AGE and angiotensin II (Ang II) has been proposed in the pathogenesis of accelerated atherosclerosis in diabetes, we examined here whether and how telmisartan, a unique Ang II type 1 receptor blocker (ARB) with peroxisome proliferator-activated receptor-gamma (PPAR-gamma)-modulating activity, could inhibit AGE-induced CRP expression in a human hepatoma cell line, Hep3B cells. **METHODS:** Protein levels of the receptor for AGE (RAGE) were analysed by western blots. Gene expression was analysed by quantitative real-time RT-PCR. CRP released into the medium was measured with ELISA. Intracellular formation of reactive oxygen species (ROS) was measured using the fluorescent probe CM-H(2)DCFDA. **RESULTS:** Telmisartan, but not candesartan, another ARB, downregulated RAGE mRNA levels in a dose-dependent manner. Telmisartan decreased basal as well as AGE-induced RAGE protein expression in Hep3B cells. Furthermore, telmisartan dose-dependently inhibited AGE-induced ROS generation and subsequent CRP gene and protein induction in Hep3B cells. GW9662, an inhibitor of PPAR-gamma, blocked the inhibitory effects of telmisartan on RAGE expression and its downstream signalling in Hep3B cells. **CONCLUSIONS/INTERPRETATION:** Our present study indicates a unique beneficial aspect of telmisartan: it may work as an anti-inflammatory agent against AGE by suppressing RAGE expression via PPAR-gamma activation in the liver and may play a protective role in vascular injury in diabetes.

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