BMC Pharmacology

Meeting abstract

Advanced oxidation protein products are antagonists of the HDL receptor SR-BI

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from 15th Scientific Symposium of the Austrian Pharmacological Society (APHAR) Joint meeting with the Hungarian Society of Experimental and Clinical Pharmacology (MFT) and the Slovenian Pharmacological Society (SDF)
Graz, Austria. 19-21 November 2009

Published: 12 November 2009

BMC Pharmacology 2009, **9**(Suppl 2):A7 doi:10.1186/1471-2210-9-S2-A7

This abstract is available from: http://www.biomedcentral.com/1471-2210/9/S2/A7

Background

Advanced oxidation protein products (AOPPs) are carried by oxidized plasma proteins, especially albumin, and are important risk factors for cardiovascular events in patients with renal disease. Renal patients have a high prevalence of coronary and carotid arteriopathy and face an excessive cardiovascular mortality. Therefore the role(s) of AOPPs in the development of cardiovascular disease might be of great importance.

Results

Herein, we demonstrate that albumin isolated from hemodialysis (HD) patients and *in vitro*-generated AOPP-albumin binds with high affinity to the high-density lipoprotein (HDL) receptor scavenger receptor class B type-I (SR-BI). AOPP-albumin blocked HDL association to SR-BI and effectively inhibited SR-BI-mediated cholesterol ester (CE) uptake, dependent on the AOPP content of albumin. Furthermore, we demonstrate that AOPP-albumin effectively reduces SR-BI-mediated lipid tracer uptake in mice. AOPP-albumin administration increased the plasma half-life of [^{3}H]CE-HDL in control mice 1.6-fold ($p = 0.01$) and 8-fold ($p = 0.0003$) in mice infected with adenoviral vectors encoding human SR-BI.

Conclusion

The observed inhibitory activity of albumin isolated from HD patients is of clear physiological relevance. Our data indicate that a physiological molar excess of HD-albumin over HDL may block up to 50% of HDL-CE delivery to SR-BI. Summing up, we provide strong *in vivo* and *in vitro* evidence that AOPPs are proinflammatory mediators that directly impair HDL metabolism and might therefore be potential key players in the development of cardiovascular disease.