

Dietary supplementation with tetradecylthioacetic acid or a salmon protein hydrolysate reduces atherosclerosis progression in apoE-KO mice

E. Deller¹, M. Busnelli¹, G.S. Ganzetti¹, S. Manzini¹, R. Vik², T. Brattelid², B. Bjørndal², C.R. Sirtori¹, R.K. Berge², C. Parolini^{1*}, G. Chiesa^{1*}

¹Dept of Pharmacological and Biomolecular Sciences, Università degli Studi di Milano, Milan, Italy

²Institute of Medicine, University of Bergen, 5021 Bergen, Norway

* *The authors equally contributed to this work.*

Atherosclerosis is a complex vascular disease with a bidirectional interaction between lipids and inflammation as a major feature. These interactions involve macrophages/monocytes, T cells, vascular smooth muscle cell and endothelial cells, and in addition to inflammation and lipid deposition, matrix remodelling is an important characteristic of the atherosclerotic lesion. Tetradecylthioacetic acid (TTA) is a synthetic long-chain fatty acid analogue with marked hypolipidemic and anti-inflammatory effects. These combined effects are of particular interest in view of a potential anti-atherogenic activity. Fish peptides (fish protein hydrolysate containing mixed peptides lower than MW 10,000) have shown to have hypolipidemic effects and thus may slow the progression of atherosclerosis. Aim of the study was to investigate the effect of TTA and of a salmon protein hydrolysate on atherosclerosis progression in apoE-KO mice. 36 apoE-KO mice have been randomly divided in three groups and fed for 12 weeks a high-fat diet alone (control) or supplemented with 0.3% TTA and 5% salmon protein hydrolysate (g/100g of diet). At sacrifice, aortic arch and heart have been harvested and processed to perform en-face and histological analysis, respectively. Compared to the control group, TTA supplementation led to a significantly reduced atherosclerotic plaque area in the aortic arch (-77.7% vs. control; $p < 0.05$) and displayed a trend towards a lower plaque development in the aortic sinus (-25.9% vs. control; $p = 0.068$). Salmon protein hydrolysate supplementation led to a significantly reduced plaque development at both the aortic arch (-66.6% vs. control; $p < 0.05$) and the aortic sinus (-36.9% vs. control; $p < 0.05$). In conclusion, the present study demonstrated that a supplementation with 0.3% TTA reduced atherosclerotic plaque development in high-fat fed apoE-KO mice, particularly at the aortic arch. Moreover, supplementation with 5% salmon protein hydrolysate significantly reduced atherosclerotic lesion progression at both the aortic sinus and the aortic arch.