ABSTRACT

Statins are widely used for their eminent hypolipidemic effect as anti-atherosclerotic drugs from the 90's of the 20th century. Even though there are new approaches, statins are still the first choice in the prevention of cardiovascular diseases. At the beginning of the 21st century, the anti-inflammatory effect independent of lipid-lowering properties was discovered.

This diploma thesis deals with the effect of statin treatment on macrophage polarisation *in vitro*. Macrophages differentiated from blood monocytes were used in this thesis. The effect of statin treatment on the expression of surface markers (CD16, CD15, CD36, CD163, CD206, ABCA-1 and Trem-2) was evaluated by flow cytometry. The qPCR method was used to quantify the effect of statin treatment
on the gene expression of inflammatory genes (NFκB, IL-1β, IL-6, TNFα and iNOS), anti-inflammatory genes (Arg-1, TGFβ) and genes which play a role in the adhesion and migration of monocytes
and macrophages to vessel intima (VCAM-1 and MCP-1). Griess method was used to evaluate the effect of statin treatment on the inducible NO-synthase activity. Last, but not least, the effect of statin treatment
on proteosynthesis of inflammatory cytokines (IL-1β, IL-6 a TNFα) and anti-inflammatory cytokine IL-10 was measured.

Flow cytometry results show that statins decrease the expression of CD15, CD36, ABCA-1, Trem-2 and CD163. The expression of CD206 was significantly increased on M2 macrophages under the statin treatment. qPCR analysis showed a significant effect of statin therapy on reducing the gene expression of the inflammatory markers NFκB, IL-1β, IL-6 and iNOS in M1 macrophages, enhancing the expression of anti-inflammatory markers Arg-1 and TGFβ. The gene expression of VCAM-1 and MCP-1 was also altered. The significant effect of statins on the iNOS activity in M1 macrophages was proved by Griess method. This result is congruent with the gene expression analysis results. Finally, the levels of pro-inflammatory cytokines IL-1β, IL-6 and TNFα released by all macrophage subtypes were reduced under the statin treatment. The production of anti-inflammatory cytokine IL-10 by M1 and M2 macrophages was significantly elevated under the statin treatment.

The results presented in this thesis prove the anti-inflammatory effect of statins on the inflammatory markers and prove the direct ability of statins to enhance the expression and/or production of markers connected with the anti-inflammatory phenotype of immune reaction. This thesis contributes to a closer understanding of the effect of statin therapy on the inflammatory profile of macrophages and expand current knowledge about the anti-inflammatory effect of statins regardless of their hypolipidemic ability.