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ANTI-INFLAMMATORY AND ANTI-ATHEROGENIC EFFECTS OF ACETYL-11-KETO-b-BOSWELLIC ACID IN LPS-CHALLENGED APOLIPOPROTEIN E-DEFICIENT MICE

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Objectives- Micro-organisms might play a role in chronic inflammatory disease such as atherosclerosis. We studied the effect of acetyl-11-keto-b-boswellic acid (AKbBA), a molecule isolated from the gum resins of various *Boswellia* species, on atherosclerotic lesion development in apolipoprotéin E deficient (apoE$^{-/-}$) mice. **Methods-**Atherosclerotic lesions were induced by weekly lipopolysaccharide (LPS) injection in apoE$^{-/-}$ mice to mimic chronic inflammation. **Results-** Our results showed that LPS alone increases atherosclerotic lesion size and that the treatment with AKbBA-cyclodextrin significantly reduced it (~50 % reduction vs. control (100%), n=8, $p<0.001$). Moreover, the activity of the nuclear transcription factor NF-kB was also reduced in LPS-injected apoE$^{-/-}$ mice and treated with AKbBA-cyclodextrin as judged by the increase of the IkBa in the cytosol and the decrease of nuclear staining of the p65 subunit. As a consequence, a significant down-regulation in the expression of several genes, among which MCP-1, MCP-3, IL-1a, MIP-2, VEGF and TF was observed. By contrast, neither g-cyclodextrin nor AKbBA-cyclodextrin complex were able to affect the plasma concentration of triglycerides, total cholesterol, anti-oxidized LDL antibodies and various subset of lymphocyte-derived cytokines. **Conclusion-** The inhibition of NF-kB activity by plant resins from species of the *Boswellia* family might represent an alternative for classical medicine treatments for chronic inflammatory diseases such as atherosclerosis.

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THE MIAMI STUDY (MARKERS OF INFLAMMATION AND ATORVASTATIN EFFECT IN PREVIOUS MYOCARDIAL INFARCTION): RESULTS OF A PROSPECTIVE, OPEN-LABEL, MULTICENTER STUDY

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Objective: To investigate the relationship between changes induced by atorvastatin in carotid IMT (C-IMT) and changes in soluble markers of inflammation, thrombosis and endothelial function. **Methods**: Patients with stable ischemic heart disease (n=85) were treated with 20 mg/day of atorvastatin for 20±4 months. C-IMT, soluble markers (sVCAM-1, sICAM-1, sE-selectin, IL-6, IL-8, IL-18, TNFα, hsCRP, vWF, CD40L, MMP9, fibrinogen) and lipids were measured at times 0, 12 and 24 months. **Results:** Atorvastatin induced C-IMT regression ($p=0.004$ for IMT_{mean}) and significantly reduced plasma levels of triglycerides, total-C, LDL-C, vWF, sICAM-1, sE-selectin, fibrinogen (all $p<0.0001$), IL-8 ($p=0.004$), MMP9 and TNFα (both $p<0.05$). HDL-C, IL-6 and CD40L increased in response to therapy ($p<0.05$), whereas hsCRP, IL-18, and sVCAM-1 did not change. Changes in lipids and in soluble markers were poorly correlated with C-IMTs changes when analyzed singly. In contrast, the combination of changes in soluble markers (soluble marker-score), soluble markers and lipids (total-score) or biologically-related variables (inflammatory-score, interleukin-score and adhesion molecule-score) strongly correlated with the effects of atorvastatin on carotid IMT ($p=$ 0.007, 0.002, 0.04, 0.003 and 0.17, respectively). **Conclusion:** The anti-atherosclerotic effect of atorvastatin could be explained, at least in part, by pleiotropic effects on markers of inflammation, thrombosis and endothelial dysfunction.

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