Effects of free curcumin and curcumin-liposomes (*lipocurc^{TM}*) on pro-inflammatory cytokine expression in synovial fibroblasts and macrophages

Lukas Gober, Silvia Löbsch, Lawrence Helson, Andreas Wagner, Günter Steiner, Burkhard Klösch

Background and aim: The polyphenolic compound curcumin, which naturally occurs in the rhizome of the plant *Curcuma longa*, has been shown to have potent anti-inflammatory and anti-cancer properties. Its pharmacological application remains limited due to its extremely low water solubility and bioavailability. To bypass these problems, a novel nanocarrier system termed ***lipocurc^{TM}*** was developed by Polymun Scientific (Klosterneuburg, Austria) and kindly provided by Signpath Pharma (Center Valley, USA). In the present study, we compared the effects of free curcumin (Signpath Pharma) and *lipocurc^{TM}* on the proliferation and pro-inflammatory cytokine expression of two different cell types.
Methods: Human synovial fibroblasts (SW982 cell line) were treated with different concentrations of free curcumin or *lipocurc^{TM}* for 24 or 48 h before being stimulated with IL-1β to induce IL-6/IL-8 expression. Murine macrophages (RAW264 cell line) were treated as described above and were stimulated with LPS to induce TNF-α/IL-6 expression. In addition, the effects of free curcumin and *lipocurc^{TM}* on the proliferation of synovial fibroblasts and macrophages were investigated. In all experiments, empty liposomes served as a negative control. IL-6/IL-8/TNF-α release was quantified by ELISA, cell proliferation was monitored by XTT-assay.
Results: Pre-treatment with free curcumin or *lipocurc^{TM}* for 24 or 48 h significantly downregulated IL-6/IL-8 expression in SW982 cells as well as IL-6/TNF-α expression in RAW264 cells. Interestingly, empty liposomes significantly downregulated IL-6/TNF-α expression in RAW264 cells, whereas no inhibitory effects were observed in SW982 cells. Free curcumin led to a significant time- and dose-dependent reduction of the proliferation rate in both cell types. *Lipocurc^{TM}* decreased the proliferation rate of RAW264 cells, whereas no negative effects were observed in SW982 cells. Empty liposomes had no negative effects on the proliferation of both cell lines.
To conclude, our study demonstrate that free curcuimin and *lipocurc^{TM}* have similar effects on pro-inflammatory cytokine expression in SW982 and RAW264 cells.