The polyphenols curcumin and resveratrol effectively block IL-1β and PMA-induced IL-6 and VEGF-A expression in human synovial fibroblasts

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Background and objectives: Polyphenols such as curcumin and resveratrol have a wide range of pharmacological and biological activities. The anti-oxidant, anti-inflammatory and apoptotic effects of these compounds have been assessed in various in vitro and in vivo systems. Several studies have reported curcumin and resveratrol to modulate numerous aspects of the cell function relevant to inflammatory arthritis (RA). In RA, most of the production of cytokines and chemokines such as TNF-α, IL-1β, IL-6 and IL-8 has been attributed to two main cell types; macrophages and synovial fibroblasts (FLS). This study investigated the anti-inflammatory effects of curcumin and resveratrol on the human rheumatoid fibroblast cell line MH7A and FLS derived from RA patients. Particular attention was paid to the modulation of IL-6 and VEGF-A expression and activation of caspases by these substances.

Co-treatment of FLS with IL-1β and curcumin or resveratrol prevents upregulation of IL-6 expression

MH7A cells and RA-FLS (RA 26) were left untreated or were incubated for 6 h with IL-1β in the absence or presence of increasing concentrations of curcumin (12.5 - 50 µM) or resveratrol (12.5 - 100 µM). Afterwards, the cell culture supernatants were collected and IL-6 levels were quantified by enzyme-linked immunosorbent assay (ELISA; A, B MH7A cells; C, D RA-FLS (RA 28).

Curcumin and resveratrol block PMA-induced IL-6 expression

MH7A cells and RA-FLS (RA 26) were left untreated or were incubated for 6 h with IL-1β, IL-6 and IL-8 has been attributed to two main cell types; macrophages and synovial fibroblasts (FLS). This study investigated the anti-inflammatory effects of curcumin and resveratrol on the human rheumatoid fibroblast cell line MH7A and FLS derived from RA patients. Particular attention was paid to the modulation of IL-6 and VEGF-A expression and activation of caspases by these substances.

Curcumin and resveratrol inhibit PMA-induced VEGF-A expression in RA-FLS

RA-FLS (RA 26) were treated as described above and VEGF-A levels were quantified by ELISA.

Curcumin induces activation of caspase 9

MH7A cells were incubated for 6 h with increasing concentrations of curcumin (12.5 - 50 µM) and activation of caspases (3, 7 and 9) was analysed by Western blotting.

Resveratrol does not block lκBα degradation but deactivates ERK1/2

MH7A cells were incubated for 60 min with increasing concentrations of resveratrol (12.5 - 100 µM) before being stimulated for 20 min with IL-1β (10 ng/ml).

Conclusion: Curcumin and resveratrol are natural compounds representing strong anti-inflammatory effects. In FLS, IL-6 expression was dramatically downregulated when cells were co-treated with IL-1β and curcumin or resveratrol. Curcumin prevents degradation of lκBα and initiates rapid dephosphorylation of ERK1/2. Resveratrol does not block lκBα degradation but deactivates ERK1/2. Furthermore, we found that curcumin induces activation of caspase 9. Taken together we postulate that both substances could play a role in the treatment of chronic inflammatory disorders, like RA.