13 THE POLYPHENOLS CURCUMIN AND RESVERATROL EFFECTIVELY BLOCK IL-1β AND PMA-INDUCED IL-6, IL-8 AND VEGF-A EXPRESSION IN HUMAN RHEUMATOID SYNOVIAL FIBROBLASTS

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Background and objectives Polyphenols such as curcumin (diferuloylmethane) and resveratrol (trans-3,49,5-trihydroxystilbene) have a wide range of pharmacological and biological activities. The antioxidant, 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 tumour necrosis factor 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 a human rheumatoid fibroblast cell line (MH7A) and FLS obtained from RA patients.

Particular attention was paid to the modulation of IL-6, IL-8 and VEGF-A expression.

Materials and methods The human synovial fibroblast cell line MH7A and FLS derived from two RA patients were stimulated with IL-1β (10 ng/ml) or PMA (100 ng/ml) in the absence or presence of increasing concentrations of curcumin or resveratrol (12.5–100 μM). After 3 and 6 h, the cell culture supernatants were collected and were analysed for IL-6, IL-8 and VEGF-A release by ELISAs. Furthermore, the modulation of various MAPKs (p38, ERK1/2) and transcription factor NF-κB by these substances was investigated by immuno-blotting.

Results Both curcumin and resveratrol effectively blocked IL-6, IL-8 and VEGF-A expression in RA-FLS in a concentration dependent manner. Notably, VEGF-A expression was only induced by PMA, but not by IL-1β and could be detected only 6 h after stimulation. In the cell line MH7A however, VEGF-A expression was not detectable. Both substances prevented activation of MAPKs and NF-κB in all cell populations.

Conclusion Curcumin and resveratrol are natural compounds representing strong anti-inflammatory effects and could play a role in the treatment of chronic inflammatory diseases like RA.