Chemopreventive effects of a curcumin-like diarylpentanoid [2,6-bis(2,5-dimethoxybenzylidene)cyclohexanone] in cellular targets of rheumatoid arthritis in vitro

ABSTRACT

Aim: Synovial fibroblast has emerged as a potential cellular target in progressive joint destruction in rheumatoid arthritis development. In this study, BDMC 33 (2,6-bis[2,5-dimethoxybenzylidene]cyclohexanone), a curcumin analogue with enhanced anti-inflammatory activity has been synthesized and the potency of BDMC 33 on molecular and cellular basis of synovial fibroblasts (SF) were evaluated in vitro.

Methods: Synovial fibroblast cells (HIG -82) were cultured in vitro and induced by phorbol-12-myristate acetate (PMA) to stimulate the expression of matrix metalloproteinase (MMP s) and pro-inflammatory cytokines. The protective effects of BDMC 33 were evaluated toward MMP activities, pro-inflammatory cytokine expression and nuclear factor kappa-B (NF -κB) activation by using various bioassay methods, including zymography, Western blotting, reverse transcription polymerase chain reaction, immunofluorescense microscopy and electrophoretic mobility shift assay.

Results: The results showed that BDMC 33 significantly inhibited the pro-gelatinase B (pro-MMP -9) and collagenase activities via suppression of MMP -1 in activated SF. In addition, BDMC 33 strongly suppressed MMP-3 gene expression as well as inhibited COX-2 and IL-6 pro-inflammatory gene expression. We also demonstrated that BDMC 33 abolished the p65 NF-κB nuclear translocation and NF-κB DNA binding activity in PMA -stimulated SF.

Conclusions: BDMC33 represents an effective chemopreventive agent and could be used as a promising lead compound for further development of rheumatoid arthritis therapeutic intervention.

Keyword: BDMC33; Curcumin; HIG-82; Matrix metalloproteinase; NF-κB; Synovial fibroblast