

Acanthopanax koreanum and Major Ingredient, Impressic Acid, Possess Matrix Metalloproteinase-13 Down-Regulating Capacity and Protect Cartilage Destruction

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Abstract : Matrix metalloproteinase (MMP)-13 has an important role for degrading cartilage materials under inflammatory conditions such as arthritis. Since the 70% ethanol extract of *Acanthopanax koreanum* inhibited MMP-13 expression in IL-1 β -treated human chondrocyte cell line, SW1353, two major constituents including acanthoic acid and impressic acid were initially isolated from the same plant materials and their MMP-13 down-regulating capacity was examined. In IL-1 β -treated SW1353 cells, acanthoic acid and impressic acid significantly and concentration-dependently inhibited MMP-13 expression at 10 - 100 μ M and 0.5 - 10 μ M, respectively. The potent one, impressic acid, was found to inhibit MMP-13 expression by blocking the phosphorylation of signal transducer and activator of transcription-1/-2 (STAT-1/-2) and activation of c-Jun and c-Fos among cellular signaling pathway involved, but did not affect the activation of mitogen-activated protein kinases (MAPKs) and nuclear transcription factor- κ B (NF- κ B). Further, impressic acid was also found to inhibit the expression of MMP-13 mRNA (47.7% inhibition at 10 μ M), the glycosaminoglycan release (42.2% reduction at 10 μ M) and proteoglycan loss in IL-1-treated rabbit cartilage explants culture. For a further study, 21 impressic acid derivatives were isolated from the same plant materials and their suppressive activities against MMP-13 expression were examined. Among the derivatives, 3 α -hydroxy-lup-20(29)-en-23-oxo,28-oic acid, (20R)-3 α -hydroxy-29-dimethoxylupan-23,28-dioic acid, acankoreoside F and acantrifoside A clearly down-regulated MMP-13 expression, but impressic acid being most potent. All these results suggest that impressic acid, 3 α -hydroxy-lup-20(29)-en-23-oxo,28-oic acid, (20R)-3 α -hydroxy-29-dimethoxylupan-23,28-dioic acid, acankoreoside F, acantrifoside A and *A. koreanum* may have a potential for therapeutic agents to prevent cartilage degradation possibly by inhibiting matrix protein degradation.

Keywords : acanthoic acid, *Acanthopanax koreanum*, cartilage, impressic acid, matrix metalloproteinase

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