World Academy of Science, Engineering and Technology
International Journal of Biomedical and Biological Engineering
Vol:11, No:05, 2017

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-1β-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-1β-treated SW1353 cells, acanthoic acid and impressic acid significantly and concentration-dependently inhibited MMP-13 expression at 10 – 100 μM and 0.5 – 10 μM, 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-κB (NF-κB). Further, impressic acid was also found to inhibit the expression of MMP-13 mRNA (47.7% inhibition at 10 μM), the glycosaminoglycan release (42.2% reduction at 10 μM) 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, 3α-hydroxy-lup-20(29)-en-23-oxo,28-oic acid, (20R)-3α-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, 3α-hydroxy-lup-20(29)-en-23-oxo,28-oic acid, (20R)-3α-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
Conference Title : ICI 2017 : International Conference on Inflammation
Conference Location : Amsterdam, Netherlands
Conference Dates : May 14-15, 2017