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Gene Regulatory Effects of Sappan lignum Extract in a Cell Model of Joint Inflammation

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In recent years, intraarticular inflammation has been recognized to contribute to the symptoms and progression of osteoarthritis (OA). Inflammation in OA is associated with increased levels of catabolic enzymes and inflammatory mediators such as nitric oxide (NO), interleukin-1ß (IL-1ß) and tumor necrosis factor-α (TNF-α). Chondrocytes and infiltrating inflammatory cells, neurtrophils and macrophages, participate in the production of these catabolic mediators [1]. Extract from the heartwood of *Caesalpinia sappan* and its active components were reported to have antioxidative, antibacterial and anti-inflammatory effects [2]. The present study was designed to investigate whether ethanolic extract of *C. sappan* possesses anti-inflammatory activities in an *in vitro* model of joint inflammation comprising primary human osteoarthritic chondrocytes and differentiated THP-1 macrophage cells.

Using real-time quantitative PCR, we found that lipopolysaccharide caused enhanced gene expression levels of IL-1ß and TNF-α in THP-1 macrophages. Moreover, IL-1ß stimulated chondrocytes to upregulate inducible nitric oxide synthase (iNOS,), IL-1ß and TNF-α transcription. In accordance with these changes at the mRNA level, an increased NO production in IL-1ß treated chondrocytes was observed by Griess assay. Interestingly, sappanwood extract exhibited an inhibitory effect on LPS-induced cytokine expression in THP-1 cells as well as on enhanced NO synthesis and iNOS, IL-1ß and TNF-α transcription in IL-1ß stimulated chondrocytes. In addition, these effects were even promoted when cells were preincubated with sappanwood extract 1 hour before addition of LPS and IL-1ß. In conclusion, the present results suggest that sappanwood extract may be of potential therapeutic value in the treatment of OA.

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