

[PC1-24] [ 10/20/2000 (Fri) 15:30 – 16:30 / [Hall B] ]

**Ergolide, sesquiterpene lactone from *Inula britannica*, inhibits inducible nitric oxide synthase and cyclooxygenase-2 expression in RAW 264.7 macrophages through the inactivation of NF- $\kappa$ B**

Yoon JW\*, Jin HK, Kim YK, Lee BG, Zee OP, Lee KR, Lee HY#, Hong SY##, Han JW, Lee HW

College of Pharmacy, Sungkyunkwan University, College of Medicine, Konyang University#,  
College of Life Science and Natural Resources, Sungkyunkwan University##

The inhibitory effects and its mechanism of ergolide, sesquiterpene lactone from *Inula britannica*, on the expression of inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2) by lipopolysaccharide/interferon- $\gamma$  (LPS/IFN- $\gamma$ ) in RAW 264.7 macrophages were investigated. iNOS activity in cell-free extract of LPS/IFN- $\gamma$ -stimulated RAW 264.7 macrophages was markedly attenuated by the treatment with ergolide. Its inhibitory effect on iNOS was paralleled by decrease in nitrite accumulation in culture medium of LPS/IFN- $\gamma$ -stimulated RAW 264.7 macrophages in a concentration-dependent manner. Furthermore, treatment with ergolide led to a decrease in iNOS protein as well as mRNA expression levels, as measured by Western blot and Northern blot analysis. In addition, prostaglandin E<sub>2</sub> (PGE<sub>2</sub>) production as well as COX-2 expression in cell-free extract of LPS-stimulated RAW 264.7 macrophages was inhibited by the treatment with ergolide in a concentration-dependent manner. Furthermore, ergolide inhibited nuclear factor- $\kappa$ B (NF- $\kappa$ B) activation, a transcription factor necessary for iNOS and COX-2 expression in response to LPS/IFN- $\gamma$ . This effect was accompanied by the parallel reduction of nuclear translocation of subunit p65 of NF- $\kappa$ B as well as I $\kappa$ B- $\alpha$  degradation. These results demonstrate that the suppression of NF- $\kappa$ B activation by ergolide might be mediated by blockade of the degradation of I $\kappa$ B, leading to the suppression of the expression of iNOS and COX-2, which play important roles in inflammatory signaling pathway.

[PC1-25] [ 10/20/2000 (Fri) 15:30 – 16:30 / [Hall B] ]

**Suppression of Cyclooxygenase-2 and inducible Nitric Oxide Synthase Enzyme Induction from Lipopolysaccharide-induced RAW 264.7 by Wogonin, a Plant Flavone from *Scutellaria Radix***

Cheon BS, Chi YS and Kim HP

College of Pharmacy, Kangwon National University, Korea

Some flavonoids such as flavone derivatives were previously reported to inhibit nitric oxide (NO) production by suppression of inducible nitric oxide synthase (iNOS) expression. In this investigation, the effects of wogonin, one of the potent inhibitors of NO production among flavonoids tested, on cyclooxygenase-2 (COX-2) induction and COX-2 enzyme activity were further elucidated using a mouse macrophage cell line, RAW 264.7. Wogonin inhibited NO and PGE<sub>2</sub> production from lipopolysaccharide-induced RAW cells in different sensitivity (IC<sub>50</sub>: 31  $\mu$ M for NO and 0.3  $\mu$ M for PGE<sub>2</sub> production). Wogonin also inhibited COX-2 activity directly (IC<sub>50</sub>: 46  $\mu$ M) from the homogenate of aspirin-pretreated RAW cells measured by [<sup>14</sup>C]PGE<sub>2</sub> formation from [<sup>14</sup>C]arachidonic acid. However, it did not inhibit iNOS and phospholipase A<sub>2</sub> activity. Western blotting showed that wogonin suppressed the induction of both iNOS and COX-2. Therefore, wogonin is a direct COX-2 inhibitor as well as an inhibitor of iNOS and COX-2 induction, suggesting its potential use for inflammatory diseases.

[PC1-26] [ 10/20/2000 (Fri) 15:30 – 16:30 / [Hall B] ]

**Induction of Apoptosis by Ginsenoside Rc in Human Melanoma (SK-MEL-28) Cell Line**