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### Down-regulation of naringenin on iNOS, IL-1 $\beta$ and IL-6, in murine macrophages

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In this study, we investigated the effect of naringenin on the regulation of iNOS and proinflammatory cytokines, such as, IL-1 $\beta$ , IL-6, in murine macrophages. Naringenin alone did not affect the expression of iNOS and proinflammatory cytokines; in contrast, treatment of suppressed the LPS-induced gene expression of IL-1 $\beta$ , IL-6 and iNOS, in a dose-dependent manner as determined by RT-PCR analysis. NO production was assessed by measurement of nitrites in the medium. The level of NO was found to correlate well with a decrease in transcripts of iNOS. Since the promoter in IL-1 $\beta$  and iNOS gene contains binding motifs for NF- $\kappa$ B, the effect of naringenin on the inactivation of this transcripts factor was determined by transient transfection assay. Employing a transfection and reporter gene expression system with p(NF- $\kappa$ B)3-Luciferase, the treatment of naringenin produced a dose-dependent inhibition of luciferase activity in RAW 264.7 murine macrophages cell line. These results suggest that suppression of iNOS, IL-1 $\beta$ , and IL-6 gene expression by naringenin might be mediated by the inhibition of NF- $\kappa$ B activation [This work was supported by KFDA Grant and RCPM from KOSEF].

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### Suppression of nonylphenol on iNOS, IL-1 $\beta$ and IL-6 in murine macrophages

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4-Nonylphenol is a degradation product of a widely used non-ionic surfactant group, alkylphenol polyethoxylates that are mainly found as an intermediate in the chemical manufacturing industry. In this study, we investigated the effect of nonylphenol on the regulation of iNOS and proinflammatory cytokines, such as, IL-1 $\beta$ , IL-6 in murine macrophages. Nonylphenol alone did not affect the expression of iNOS and proinflammatory cytokines; in contrast, treatment of suppressed the LPS-induced gene expression of IL-1 $\beta$ , IL-6, and iNOS, in a dose-dependent manner as determined by RT-PCR analysis. NO production was assessed by measurement of nitrites in the medium. The level of NO was found to correlate well with a decrease in transcripts of iNOS. Since the promoter in IL-1 $\beta$  and iNOS gene contains binding motifs for NF- $\kappa$ B, the effect of nonylphenol on the inactivation of this transcripts factor was determined by transient transfection assay and electrophoretic mobility shift assay (EMSA). Employing a transfection and reporter gene expression system with p(NF- $\kappa$ B)3-Luciferase, the treatment of nonylphenol produced a dose-dependent inhibition of luciferase activity in RAW 264.7 murine macrophages cell line. Using DNA fragments containing the NF- $\kappa$ B binding sequence, nonylphenol was shown to inhibition the protein/DNA binding of NF- $\kappa$ B to its cognate site as measured by EMSA. These results suggest that suppression of iNOS, IL-1 $\beta$ , and IL-6 gene expression by Nonylphenol might be mediated by the inhibition of NF- $\kappa$ B activation [This work was supported by KFDA Grant and RCPM from KOSEF].

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### Suppression of bisphenol A on iNOS, IL-6 and TNF- $\alpha$ in murine macrophages