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Anti-inflammatory effect of *Lonicera caerulea* through ATF3 and Nrf2/HO-1 Activation in LPS-stimulated RAW264.7 Cells

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In this study, we evaluated the anti-inflammatory effect of extracts of leaves (LCLE) and branches (LCBE) from L. caerulea in LPS-stimulated RAW264.7 cells. Inhibitory effect of LCLE and LCBE against LPS-induced overproduction of NO, iNOS and IL-1β was higher than LCFE. Furthermore, LCLE and LCBE significantly inhibited the overexpression of COX-2, IL-6 and TNF-α in LPS-stimulated RAW264.7 cells. LCLE and LCBE did not inhibited LPS-induced degradation of IκB-α, but blocked the nuclear accumulation of p65. LCLE did not inhibited LPS-induced phosphorylation of ERK1/2 and p38, while LCBE significantly attenuated phosphorylation level of p38. LCLE and LCBE increased HO-1 protein level and decrease of iNOS and IL-1β expression by LCLE and LCBE was inhibited by HO-1 knockdown. The inhibition of p38 by SB203580 and ROS by NAC blocked HO-1 expression by LCLE and LCBE. LCLE and LCBE increased p38 phosphorylation and the inhibition of ROS by NAC blocked p38 phosphorylation LCLE and LCBE. LCLE and LCBE induced nuclear accumulation of Nrf2, but this was significantly reversed by the inhibition of p38 and ROS. In addition, LCLE and LCBE increased ATF3 expression and decrease of iNOS and IL-1β expression by LCLE and LCBE was inhibited by ATF3 knockdown. Collectively, LCLE and LCBE inhibited LPS-induced NF-κB activation by blocking p65 nuclear accumulation, increased HO-1 expression by ROS/p38/Nrf2 activation, and increased ATF3 expression. Furthermore, LCBE inhibited LPS-induced p38 phosphorylation.

Key words: Anti-inflammation, Inflammatory response, *Lonicera caerulea*, Macrophage

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