F-P-8

Inhibitory Effect of *Sageretia theezans* against the Production of Pro-Inflammatory Mediators through the Inhibition of NF-κB and MAPK, and Activation of Nrf2/HO-1 Signaling Pathways in LPS-Stimulated RAW264.7 cells

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In this study, we evaluated the anti-inflammatory effect of extracts of leaves (ST-L) and branches (ST-B) from *Sageretia theezans* in LPS-stimulated RAW264.7 cells. ST-L and ST-B significantly inhibited the production of the pro-inflammatory mediators such as NO, iNOS, COX-2, IL-1β and IL-6 in LPS-stimulated RAW264.7 cells. ST-L and ST-B blocked LPS-induced degradation of IκB-α and nuclear accumulation of p65, which resulted to the inhibition of NF-κB activation in RAW264.7 cells. ST-L and ST-B also attenuated the phosphorylation of ERK1/2, p38 and JNK in LPS-stimulated RAW264.7 cells. In addition, ST-L and ST-B increased HO-1 expression in RAW264.7 cells, and the inhibition of HO-1 by ZnPP reduced the inhibitory effect of ST-L and ST-B against LPS-induced NO production in RAW264.7 cells. Inhibition of p38 activation and ROS elimination attenuated HO-1 expression by ST-L and ST-B, and ROS elimination inhibited p38 activation induced by ST-L and ST-B. ST-L and ST-B dramatically induced nuclear accumulation of Nrf2, but this was significantly reversed by the inhibition of p38 activation and ROS elimination. Collectively, our results suggest that ST-L and ST-B exerts potential anti-inflammatory activity by suppressing NF-κB and MAPK signaling activation, and activating HO-1 expression through the nuclear accumulation of Nrf2 via ROS-dependent p38 activation. These findings suggest that ST-L and ST-B may have great potential for the development of anti-inflammatory drug to treat acute and chronic inflammatory disorders.

Keywords: Anti-inflammation; Inflammatory response; Macrophage; *Sageretia theezans*

[This work was supported by Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education (NRF-2016R1D1A3B03931713 and NRF-2018R1A6A1A03024862).]