## Ginseng extract and total saponins suppress microglial activation in vitro and in vivo: implications for the treatment of Alzheimer's disease

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The microglial activation plays an important role in the pathogenesis of Alzheimer's disease by producing neurotoxic factors such as proinflammatory cytokines and nitric oxide (NO). Therefore, the inhibition of microglial activation would be an effective therapeutic approach to alleviating the progression of Alzheimer's disease. In the present study, we investigated the effect of Korea Red Ginseng on microglial activation. Ginseng extract and total saponins suppressed LPS-induced release of NO, TNF- $\alpha$ , and IL-6 in BV2 microglial cells. The inhibitory effect of total saponins was more potent than that of ginseng extract, suggesting that the main effective constituents harboring anti-inflammatory activity of red ginseng may be saponins. Similarly, ginseng extract and total saponins also suppressed A $\beta$ -induced TNF- $\alpha$  and IL-1 $\beta$  expression in microglial cells. RNase protection assay showed that ginseng extract and total saponins regulated iNOS, MMP-9 and the cytokines at transcriptional level. Further mechanistic studies revealed that ginseng extract and total saponins significantly inhibited the MAPK and NF- $\kappa$ B activities in LPS-stimulated microglial cells. Finally, the inhibitory effect of ginseng extract and total saponins on microglial activation was confirmed in LPS-injected mice. Therefore, the inhibition of microglial activation by ginseng extract and total saponins might have therapeutic potential for Alzheimer's disease and other neurodegenerative diseases.

Keywords: Alzheimer's disease, microglia, red ginseng, cytokine, iNOS, signaling pathway