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Vaccinium oldhamii Stems Inhibit Pro-inflammatory Response and Osteoclastogenesis through Inhibition of NF-κB and MAPK/ATF2 Signaling Activation in LPS-stimulated RAW264.7 Cells

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Vaccinium oldhamii (*V. oldhamii*) has been reported to exert a variety of the pharmacological properties such as anti-oxidant activity, anti-cancer activity, and inhibitory activity of α-amylase and acetylcholinesterase. However, the anti-inflammatory activity of *V. oldhamii* has not been studied. In this study, we aimed to investigate anti-inflammatory activity of the stem extracts from *V. oldhamii*, and to elucidate the potential mechanisms in LPS-stimulated RAW264.7 cells. Among VOS, VOL and VOF, the inhibitory effect of NO and PGE2 production induced by LPS was highest in VOS treatment. Thus, VOS was selected for the further study. VOS dose-dependently blocked LPS-induced NO and PGE2 production by inhibiting iNOS and COX-2 expression, respectively. VOS inhibited the expression of pro-inflammatory cytokines such as IL-1β, IL-6 and TNF-α. In addition, VOS suppressed TRAP activity and attenuated the expression of the osteoclast-specific genes such as NFATc1, c-FOS, TRAP, MMP-9, cathepsin K, CA2, OSCAR and ATPv06d2. VOS inhibited LPS-induced NF-κB signaling activation through blocking IκB-α degradation and p65 nuclear accumulation. VOS inhibited MAPK signaling activation by attenuating the phosphorylation of ERK1/2, p38 and JNK. Furthermore, VOS inhibited ATF2 phosphorylation and blocked ATF2 nuclear accumulation. From these findings, VOS has potential to be a candidate for the development of chemopreventive or therapeutic agents for the inflammatory diseases.

Key words: Anti-inflammation, Anti-osteoclastogenesis, Inflammatory diseases, *Vaccinium oldhamii*

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