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6,8-Diprenylgenistein, an isoflavonoid isolated from *Cudrania tricuspidata* fruit inhibits VEGF-A-induced lymphangiogenesis and metastasis in an oral cancer sentinel lymph node animal model

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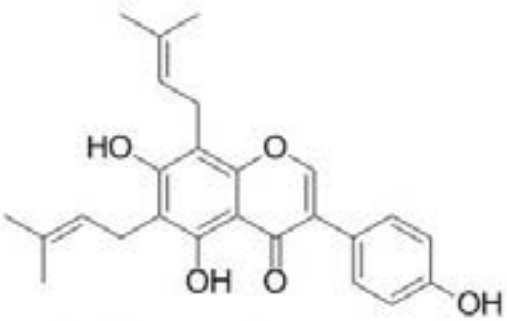
Lymphatic system is very important route of oral cancer metastasis. The presence or absence of metastasis to sentinel lymph node, first lymph node to receive cells from primary tumor through lymphatic vessels, is crucial determinant in OSCC's staging, prognosis, and treatment. We investigated the inhibitory effects of 6,8-diprenylgenistein, an isoflavonoid isolated from *Crudrania tricuspidata* fruit, on VEGF-A-induced lymphangiogenesis and lymph node metastasis both *in vitro* and *in vivo*. 6,8-Diprenylgenistein inhibited the proliferation, migration, and tube formation of human lymphatic endothelial cells (HLECs). We performed the VEGF-A-induced *in vivo* Matrigel plug assay. 6,8-Diprenylgenistein inhibited lymphatic vessel formation in VEGF-A-induced Matrigel plug. 6,8-Diprenylgenistein suppressed the activation of vascular endothelial growth factor receptor (VEGFR) -1 and -2 stimulated by VEGF-A. Also 6,8-diprenylgenistein suppressed the activation of signaling factors such as FAK, PI3K, AKT, ERK and p38 involved in VEGF-A induced lymphangiogenesis related signaling pathway. To investigate the *in vivo* effect of 6,8-diprenylgenistein on VEGF-A-induced lymphangiogenesis and lymph node metastasis, we used an oral cancer sentinel lymph node animal model. 6,8-Diprenylgenistein inhibited VEGF-A-induced lymphangiogenesis and sentinel lymph node metastasis in the animal model. Taken together, these results indicate that 6,8-diprenylgenistein has the inhibitory effects on VEGF-A-induced lymphangiogenesis and lymph node metastasis. And these results suggest that 6,8-diprenylgenistein can be a useful agent for developing new anti-cancer therapeutics. This study was supported by the Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education, Science and Technology (NRF-2016R1A6A3A11933134).



6,8-diprenylgenistein

Biography

Mun Gyeong Bae is Ph. D. candidate (M. S. & Ph. D. combined program), Graduate school of biotechnology, Kyung Hee University, Republic of Korea. Her thesis topic is identification of new natural compounds that inhibit lymph node metastasis, a major metastatic process of oral cancer, and investigation of the mechanism of inhibition of natural compounds using lymphatic endothelial cells and an oral cancer sentinel lymph node animal model.

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