

Study the Immunomodulatory Activity of Lonicerae Flos and Identify the Active Constituents

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Dendritic cells (DCs) are critical to connect innate and adaptive immunity and therefore are important targets in discovering immunomodulators. In this study, we found that the methanol extract of Lonicerae Flos (MELF), a traditional Chinese medicine, activates mouse bone marrow-derived DCs as it increases TNF- α production of the DCs treated with MELF. To investigate the active compound(s), MELF was further partially separated by partition with water and ethyl acetate, and the effects of these two layer extracts on DCs were determined. The water layer extract exhibited an activity to activate DCs; however, the ethyl acetate layer extract suppressed the activation of LPS-stimulated DC activity. These results indicated that the water layer extract contains immunostimulator(s) and ethyl acetate layer extract contains immunosuppressor(s). The constituents within the water extract were further analyzed by HPLC and we found that chlorogenic acid is the major compound. Furthermore, we confirmed that chlorogenic acid possesses an activity to activate DCs. The findings in this study are the first time to show that MELF and chlorogenic acid can activate DCs, and thus they can potentially be applied to activate DC function and increase immune responses in immunotherapy. In addition, the ethyl acetate layer extract and its immunosuppressor(s) may have potential in the treatment of chronic inflammatory and autoimmune diseases.

Novel Bioefficacy and Mechanistic Insights of the Medicinal Fungus *Antrodia Cinnamomea* against ER(+) Human Breast Cancer Cells

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Antrodia cinnamomea (AC) is a precious medicinal fungus endemic to Taiwan, which has been used anecdotally as a folk remedy for cancer diseases, diarrhea, hypertension, and hepatoprotection in Asian countries. Breast cancer is one of the top life threatening diseases in women worldwide. The objective of this study was to provide science-based evidences for the bioefficacy of fruiting body extracts of AC against human estrogen receptor positive (ER+) T47D breast cancer cell activities. The ethanolic extracts from 3-month-cultured AC fruiting bodies, designated AC-3E, observed with most significant activity against T47D cells among the tested extracts from different growth stages were employed for the pharmacological activities and molecular mechanisms investigations in vitro and in xenograft BALB/c nude mouse system. AC-3E were observed to attenuate in vitro and in vivo proliferation, migration, and tumor growth of T47D breast cancer cells by deregulating signaling pathway PI3K/Akt/mTOR and cell-cycle mediators, and induction of apoptosis. AC-3E was also functioned as an anti-angiogenic agent against blood vessel branching and microvessel formation ex vivo and in vivo. Chemical fingerprinting and cytotoxicity assay results indicate that the lanostane-type triterpenoid dehydroeburicoic acid (2) is the major bioactive compound in AC-3 extracts, which can serve as the index compound for quality control of the traditional folk medicine. This is the first report to demonstrate that AC extracts exert similarly potent activity to that of current estrogen antagonism drug tamoxifen against ER dependent T47D breast cancer cells.