The Pharmacological Potential of Apigenin and Diosmetin as a Novel Treatment for Chronic Lymphedema

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Chronic lymphedema is a progressive, disabling condition characterized by regional bodily accumulation of protein-rich interstitial fluid. It affects over 100 million worldwide, yet no pharmacological treatment exists. This novel investigation was conducted to develop the first natural pharmaceutical to treat lymphedema by examining the ability of flavonoids in vitro and ex vivo to target inflammation, abnormal lymphatic endothelial cell (LEC) layer permeability and impairment of lymphatic collecting vessel contractility that accompany lymphedema. Utilizing a new approach, 4 tests were conducted on basal and LPS-stimulated LECs, macrophages and lymphatic collecting vessels. RT-PCR assessed inflammatory gene expression (TNFa, COX-2) of cells and collecting vessels. Permeability and wound scratch assays assessed LEC layer permeability and proliferation. Pressurized vessel assays assessed lymphatic smooth muscle contractility. 1μM flavonoid treatments exhibited anti-inflammatory effects on LECs, suppressing COX-2 and TNFa when applied for 24 hours and as 2-hour pretreatments. Treatments also exhibited anti-inflammatory effects on macrophages. Apigenin reduced LEC layer permeability and promoted LEC proliferation. Apigenin restored contractility of inflamed lymphatic collecting vessels. Among many causes, the leading cause of lymphedema is filariasis, a parasitic infection threatening 1.3 billion, primarily in developing countries. Due to impoverished situations of endemic regions, physical therapy is unavailable for patients with filarial-lymphedema. Apigenin was determined to possess promising properties to target the factors that characterize lymphedema. It is low-cost and available to those in both developed countries and regions where medical support is minimal.

Awards Won:

Fourth Award of $500