8-Prenylnaringenin, a novel phytoestrogen, inhibits angiogenesis in vitro and in vivo

PROJECT: 325

1,5 Michael S. Pepper, 2 Susan J. Hazel, 3 Michael Hümpel and 3,4 Wolf-Dieter Schleuning
1 Department of Cell Biology and Morphology, University Medical Center, Geneva, Switzerland;
2 Veterinary Services Division, Institute of Medical and Veterinary Science, Adelaide, Australia;
3 Research Laboratories of Schering AG, Berlin, Germany
4 Current address: PAION GmbH Research Center, Berlin, Germany

8-prenylnaringenin is a recently discovered phytoestrogen. Using an in vitro model of angiogenesis in which endothelial cells can be induced to invade a three-dimensional collagen gel within which they form capillary-like tubes, we demonstrate that 8-prenylnaringenin inhibits angiogenesis induced by basic fibroblast growth factor (bFGF), vascular endothelial growth factor (VEGF) or the synergistic effect of the two cytokines in combination, with an IC50 of between 3-10 µM. This effect was seen with bovine microvascular endothelial cells derived from the adrenal cortex (BME cells) and with endothelial cells from the bovine thoracic aorta (BAE cells). The inhibitory effects of 8-prenylnaringenin were found to be roughly equipotent to those of genistein that has previously been shown to inhibit angiogenesis in vitro. Early CAM assay results showed reductions in both vessel lengths and vein diameters, with similar potency in the 8-prenylnaringenin and genistein groups. Similar effects on the CAM vessels were seen when the two substances were co-added. These findings suggest that 8-prenylnaringenin has potential therapeutic applications for diseases in which angiogenesis is an important component.