Abstract

Inhibition of angiogenesis represents an innovative approach to cancer chemoprevention. Therefore, we have set up a human in vitro antiangiogenic assay capable of identifying novel inhibitors of angiogenesis. In this model, fragments of superficial vessels from human placentas were cultured in fibrin gel for three weeks. Microvessel growth was monitored microscopically and quantified by computer-assisted digital image analysis. The model was evaluated using known anti-angiogenic agents acting by distinct mechanisms, i.e. indomethacin, suramin, hydrocortisone as well as the chemopreventive agents resveratrol, curcumin and (±)-epigallocatechin gallate. We utilized the established test system to evaluate the anti-angiogenic properties of a series of ten novel potential chemopreventive agents belonging to the chemical classes of phloroglucinol derivatives, anthraquinones, flavanones, diterpenes, bibenzyl derivatives of lunularic acid and chalcones. They were selected based on their potential to prevent carcinogenesis by multiple mechanisms. At concentrations up to 10µM, all of these agents potently reduced microvessel growth. The bibenzyl EC 1021 with structural similarities to resveratrol and a broad spectrum of chemopreventive mechanisms was most efficient and inhibited capillary growth by 92% at 10µM concentration. Isoxanthohumol, isoaspidinol and peracetylated carnosic acid as well as 2,2',4'-trihydroxychalcone were also identified as potent inhibitors of angiogenesis at concentrations of 10 and 1µM, respectively. Overall, we demonstrated that chemopreventive agents are an excellent repository for effective anti-angiogenic compounds and that the in vitro human anti-angiogenesis test is a valuable tool to identify these novel inhibitors. © 2004, Nova Science Publishers, Inc. All rights reserved.