

# Natural Angiogenesis Inhibitors and Cancer- Part 2.

- Dr. Pack's Summary #576
- ["Natural Health Products that Inhibit Angiogenesis: A Potential Source for Investigational New Agents to Treat Cancer-Part 2."](#)
- Curr Oncol. 2006 Jun;13(3):99-107.
- Sagar, SM., et al. Juravinski Cancer Center and McMaster University, Hamilton Ontario, Canada.

Adipocytokines are polypeptides produced by fat cells. They are associated with obesity, hyperinsulinemia, chronic vascular disease and cancer. The adipocytokines which promote angiogenesis (the growth of new blood vessels) include vascular endothelial growth factor (VEGF), hepatocyte growth factor (HGF), leptin, tumour necrosis factor alpha, heparin-binding epidermal growth factor, insulin-like growth factor and interleukin-6 (IL-6.)

Whole plant extracts contain complex chemicals with multiple targets in cells. These multiple pathways can reduce the development of multi-drug resistance in cancer cells. Over-extraction of specific plant chemicals for cancer therapy may reduce the ability of herbs to overcome multidrug resistance by the loss of synergy seen when a number of different c

hemicals act together.

Anti-angiogenic herbs block cancer growth. Curcumin (from turmeric) and epigallocatechin-3 gallate (EGCG of green tea) can inhibit aminopeptidase-N (C13,) which is an "angiogenic switch" and reduce VEGF, which increases an

giogenesis.

Epidermal growth factor receptor (EGFR) is overexpressed in many cancers and increases angiogenesis. Cancers with this overexpression are more aggressive, resist chemotherapy and have a poor prognosis. EGFR is blocked by resveratrol and quercetin. EGF is inhibited by genistein from soy and curcumin from turmeric. Resveratrol, piceatannol, curcumin, EGCG, 6-gingerol (ginger,) ursolic acid (holy basil,) and ginseng inhibit NF-KB.

COX-2 enzyme expression is increased in angiogenesis; COX-2 inhibitors block angiogenesis. The products of omega-6 fatty acid breakdown increase angiogenesis. Omega-3 fatty acids block angiogenesis. Liquorice (licorice) containing glycyrrhizic acid can inhibit COX-2 and down regulate EGF. Chemotherapy increases COX-2 as part of inflammation.

Prostaglandins derived from arachidonic acid by the action of COX enzymes act to increase angiogenesis. COX-2 inhibitors block angiogenesis. COX-2 and lipoxygenase products from omega-6 increase cancer progress by angiogenesis. Panax ginseng and curcumin are adaptogens which inhibit COX-2 and are anti-angiogenic.

Protein kinases, in normal cells, act on signals between cell wall and nucleus to regulate the cell cycles. Kinases alter cell proliferation. Some malignancies, such as chronic myelogenous leukemia and breast and bladder cancers, have been found to have mutated genes. The result is that some cancer cells have protein kinase turned on constantly with resulting constant cell division. One commonly excessive kinase is EGFR.

There are a number of plant chemicals which block protein kinase and cell signaling activity to block angiogenesis. Carnosol and ursolic acid from *Ocimum sanctum* (holy basil,) *Rosmarinus officinalis* (rosemary,) genistein and daidzein inhibit tyrosine kinases.

Bcl-2 protein controls apoptosis (cell death) and can be inhibited by curcumin, green tea extract, *Scutellaria baicalensis* (skullcap) extract, protocatechuic acid from *Hibiscus sabdariffa* (hibiscus,) EPA from fish oil, a lectin extract of *Viscum album* (mistletoe,) 6-gingerol, grape seed extract, echinocystic acid from ginseng, parthenolide from *Tanacetum parthenium* (feverfew) and beta-lapachone from *Tabebuia impetiginosa* (lapacho) tree bark.

Anticoagulants have been found to reduce metastases. Chinese destagnation herbs have anti-angiogenic and anticoagulant activity. In a study of destagnation herbs, *Salvia miltiorrhiza* (dan shen or red sage) and *Angelica sinensis* (dong quai) showed a doubling of survival rates and of the local control of tumors.

The side effects of anti-angiogenesis products are the result of angiogenesis having beneficial effects for noncancerous tissues, such as in wound healing.

**CONCLUSION:** Angiogenesis depends on multiple processes, including gene expression, signal processing, and enzyme activity. There are many natural products which block angiogenesis at multiple levels. Over-extraction of plant material can reduce that complexity and reduce the benefit of plant material, since the synergistic activity of the chemicals is beneficial.

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