Natural Angiogenesis Inhibitors and Cancer-Part 1.

- Dr. Pack's Summary #312
- "Natural Health Products that Inhibit Angiogenesis: A Potential Source for Investigational New Agents to Treat Cancer-Part 1."
- Curr Oncol. 2006 Feb;13(1):14-26.
- Sagar, SM, et al. Juravinski Cancer Center and McMaster University, Hamilton, Ontario, Canada.
- https://www.rainbow.coop/library/natural-angiogenesis-inhibitors-and-cancer-part-1/

Angiogenesis (the growth of new blood vessels) is a target for cancer therapy. Angiogenesis is necessary for cancer growth and a continued supply of oxygen and nutrition for cancers. Rapid tumor growth occurs after blood vessels develop.
Vascular endothelial growth factor (VEGF) is a protein formed by cancers which promotes angiogenesis. VEGF is, probably, essential for cancer cell migration and angiogenesis. The blood vessels formed are immature and can lead to bleeding and edema. Tumors sometimes increase angiogenesis after radiation therapy.

Angiogenesis is a normal process in the placenta, fetus and wound healing. Cancers take control of this normal process and use it without normal regulation. Dr. Judah Folkman promoted the use of anti-angiogenesis as anticancer therapy. One such pharmaceutical is bevacizumab (Avastin.) Avastin extends life when used with chemotherapy, but, has serious side effects.

Many natural products resist cancer through anti-angiogenesis combined with other processes. Chemicals which work by more than one pathway are often more effective than drugs which work by anti-angiogenesis, only. For example, heparin works by anti-angiogenesis and by anticoagulation. (Anticoagulation can reduce metastasis.)

Pharmacognosy is the science of natural drugs developed from plant medicines. Testing has been developed for screening herbs for anti-angiogenic activity. Ideally, an agent with strong anti-angiogenic activity at a low dose would reduce side effects. The new approach to chemotherapy is to use lower doses of organic chemicals which work in complementary ways.

Anti-angiogenesis products are Artemisia annua (Chinese wormwood), Viscum album (European mistletoe), Curcuma longa (turmeric), Scutellaria baicalensis (Chinese skullcap), resveratrol and proanthocyanidin (grape seed extract), Magnolia officinalis (Chinese magnolia tree), Camellia sinensis (green tea), Ginkgo biloba (ginkgo), quercetin, Poria cocos, Zingiber officinalis (ginger), Panax ginseng, Rabdosia rubescens hora (Rabdosia), and Chinese destagnation herbs. These herbs act as biologic modifiers, as adaptogens and as enhancers of conventional therapy.

Chinese wormwood (Artemisia annua) is an anti-malaria herb whose active chemical is artemisinin. It causes apoptosis (natural cell death) and lowers VEGF in cancer cells.

European mistletoe (Viscum album) is used against cancer in anthroposophic and homeopathic medicine. It lowers VEGF and induces apoptosis. One clinical cancer study seemed to show improved survival. The study had some design defects and definite conclusions could not be made.

Turmeric (Curcuma longa) contains the active ingredient, curcumin, which improves treatments with chemotherapy and radiotherapy and lowers VEGF. Nitric oxide (NO) levels correlate with tumor

growth. Curcumin reduces with cellular production of NO.

Chinese skullcap (Scutellaria baicalensis) contains baicalin and baicalcin. Skullcap is anti-angiogenic and even works against advanced prostate cancer.

Resveratrol and proanthocyanidin (grape seed extracts) from grapes and wine. They inhibit angiogenesis. One study showed that proanthocyanidin can increase angiogenesis in wound healing.

Chinese magnolia tree (Magnolia officinalis) seed cones contain honokiol blocks angiogenesis.

Milk thistle (Silybum marianum) fruit and seeds contain silibinin and silymarin. They are polyphenolic flavonoids which suppress VEGF. This has been seen in human ovarian cancer.

Green tea (Camellia sinensis) contains polyphenols and catechins which reduce breast cancer and VEGF. Epigallocatechin-3 gallate (EGCG) is a catechin comes from powdered green tea. The suggested dose is 7-8 Japanese cups (120 mL) per day. The caffeine of green tea improves anti-angiogenesis. The gastrointestinal effects and nervousness from caffeine limit the dosage.

Ginkgo (Ginkgo biloba) contains the flavonoid ginkgolide B which lowers VEGF.

Quercetin is a flavone contained in apples, raspberries, red grapes, onions, citrus fruit, cherries, broccoli and leafy green vegetables. Quercitin blocks angiogenesis and improves the anticancer effects of tamoxifen.

Poria cocos is a mushroom extract which blocks angiogenesis.

Panax ginseng contains ginsenosides which are anticancer and anti-angiogenic.

Cancer is associated with high copper levels. The cancer-promoting activity of angiogenesis is copper dependent. Copper chelation to lower copper levels is one way to treat cancer.

CONCLUSION: A number of natural products are useful in treating cancer due to their ability to reduce angiogenesis. Further clinical studies are needed. They are believed to be especially beneficial due their reduced tendency to induce resistance in cancer cells.

NOTE: Matcha is powdered Japanese green tea containing large amounts of EGCG

Natural Angiogenesis Inhibitors and Cancer-Part 2.

- Dr. Pack's Summary #576
- "Natural Health Products the 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.
- https://www.rainbow.coop/library/natural-angiogenesis-inhibitors-and-cancer-part-2/

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 curcurmin 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, protoctechuic 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.