

Clinical Pearls

This column is featured in every issue of the **Cancer Strategies Journal**, edited by **Dwight McKee, MD**. Do you have a **Clinical Pearl** that you would like to share with our readers? Please forward them to editorial@cancerstrategiesjournal.com.



From the Mederi Roundtable Discussion Group:

If patient has nausea while on orally prescribed herbs and nutrients, try having the patient take supplements after meals, and/or with ginger and citrus peel (tea and/or aroma of peel oil)

Some patients w cancer can develop high levels of 1,25 OH Vitamin D (the activated form). This can happen especially in lymphomas, and in any cancer patient who has a lot of inflammation. If CRP and/or sed rate are extremely high, make sure to run this blood test, in addition to the 25 OH Vitamin D blood test. Certain cancers, and all granulomatous tissues contain a non regulated 1-alpha hydroxylase which causes 1,25 di-OH D to go up. If the 1,25 OH Vitamin D level is too high, be careful in having a patient on oral Vitamin D supplements, because this could precipitate hypercalcemia with serious calcifications, which could show up clinically as kidney stones and worse. Many of our patients with cancer will come to us already on 5,000 IU's per day of Vitamin D, so it is important to look for this potential issue with Vitamin D supplementation. Most people with cancer do need substantial doses of Vitamin D, but care must be exercised in patients with lymphoma, or significant levels of inflammation (and in all granulomatous diseases).

Botanical compounds that either activate/up-regulate PTEN and/or inhibit PTEN mutation (important tumor suppressor gene)

Agent, source and reference:

Honokiol- from *Magnolia grandiflora/officialis*:
Eur J Pharmacol. 2008 Sep 4;591(1-3):43-51. Epub 2008 Jun 12.

Curcumin from Turmeric (*Curcuma longa*):
Cancer Res. 2010 May 1;70(9):3606-17. Epub 2010 Apr 13. *Int J Cancer.* 2009 Jul 1;125(1):1-8.

Astragalus:
Law PC, Auyeung KK, Chan LY, Ko JK. Astragalus saponins downregulate vascular endothelial growth factor under cobalt chloride-stimulated hypoxia in colon cancer cells. BMC Complement Altern Med. 2012 Sep 19;12:160. doi: 10.1186/1472-6882-12-160.

Quercetin—found in Onions, apples, and many herbs such as ginkgo biloba:
Anticancer Res. 2006 Mar-Apr;26(2A):1177-81. *Hum Mol Genet.* 2005 Jun 1;14(11):1457-63. Epub 2005 Apr 13.

Resveratrol—from Japanese Knotweed (*Polygonum cuspidatum*) and grape skin/leaf
Cell Cycle. 2008 Apr 15;7(8):1020-35. Epub 2008 Feb 15. *Review Hum Mol Genet.* 2005 Jun 1;14(11):1457-63. Epub 2005 Apr 13.

Thymoquinone- from black cumin seed (*Nigella Sativa*) oil:
Mutat Res. 2011 Jan 10;706(1-2):28-35.

Isoflavones (genistein and daidzein) from soy, red clover:
Biomed Environ Sci. 2006 Feb;19(1):35-41 *Hum Mol Genet.* 2005 Jun 1;14(11):1457-63. Epub 2005 Apr 13. *Carcinogenesis.* 2005 Oct;26(10):1793-803. Epub 2005 May 19.

Fish oil:
Breast Cancer Res Treat. 2009 Nov;118(1):213-28. Epub 2008 Oct 26.

from Donald Yance, CN, MH(AHG), Ashland, OR

Botanical compounds that target BCL2

High levels of Bcl-2 are associated with most types of human cancer. Curcumin and Green tea extract inhibit Bcl-2 expression. *Scutellaria baicalensis* extract, rich in many phenolic compounds, including baicalin, baicalein, wogonin oroxylin, was found to inhibit Bcl-2-overexpression, prostaglandin E(2) synthesis, COX-2 gene expression, and block nuclear factor-kappaB (NF-kappaB) binding and transcriptional activation. Hibiscus derived protocatechuic acid (PCA), a phenolic compound isolated from the dried flower of *Hibiscus sabdariffa* L. (Malvaceae), demonstrated antioxidant and antitumor promotion effects in part through Bcl-2 inhibition mechanism. Carnosol, a phenolic compound extracted from the herb rosemary has been reported to have anti-cancer activity. Carnosol may be useful as a novel chemotherapeutic agent against B-lineage leukemias, and possibly other types of cancers that express high levels of the protective protein, Bcl-2. 3,3'-Diindolylmethane (DIM) is a major in vivo derivative of the putative anticancer agent indole-3-carbinol (I3C), which is present in vegetables of the Brassica genus. In a recent study DIM treatment decreased total transcript and protein levels of the apoptosis inhibitory protein Bcl-2, and the amount of Bcl-2 bound to the pro-apoptotic protein Bax. Other reducers of Bcl-2 include beta-sitosterol, a main dietary phytosterol found in adaptogenic herbs and EPA from fish oil. A lectin extract of *viscum album* (mistletoe) has demonstrated an ability to induce apoptosis, by affecting Bcl-2. 6-Gingerol, a naturally occurring plant phenol, is one of the major components of fresh ginger induced cell death in promyelocytic leukemia HL-60 cells, caused DNA fragmentation and inhibited Bcl-2 expression in HL-60 cells. Grape seed extract, was also shown to regulate bcl-2 gene and downregulates the oncogene c-myc.

from Donald Yance, CN, MH(AHG), Ashland, OR

Agents targeting HIF-1a (hypoxia inducible factor alpha-1)—response to hypoxia which makes tumor cells more aggressive

Curcumin/Turmeric:
Oncol Rep. 2006 Jun;15(6):1557-62; *Mol. Pharmacol.* 2006; 70: 1664-71

Epigallocatechin-3-gallate/Green tea:
Mol. Cancer Ther. 2006; 5: 1227-38.27 4) *Mol. Cancer Ther.* 2005; 4: 1465-74

Resveratrol/Knotweed and in various fruits:
Mol. Cancer Ther. 2005; 4: 1465-74

Rapamycin/*Streptomyces hygroscopicus*:
Zhonghua Yi Xue Za Zhi 2006; 86: 1666-70

Vitexin/flavonoid compound apigenin-8-C-b-D-glucopyranoside:
Mol. Cells 2006; 22: 291-9. 2006; 86

Tocotrinal succinate /Dry Vitamin E:
J Nutr. 2008 Nov;138(11):2136-42

Silibinin (silymarin)/Milk thistle:
Oncogene (2009) 28, 313-324

Digoxin (decreases HIF-1 by 88%)/ Foxglove:
Proc Natl Acad Sci U S A. 2009 Mar 3;106(9):E26

from Donald Yance, CN, MH(AHG), Ashland, OR

Uses of Vitamin K3

Vitamin K3 can be a valuable addition to treatment protocols in integrative cancer medicine. Compounding pharmacies can make an oral sustained release vitamin K3 that can be used in combination with sustained release vitamin C in a ration of K3/ascorbate of 1:100. There's plenty of pre-clinical data supporting the 100:1 C/K3. Orally, you can go pretty high with K3--bowel tolerance to the oral ascorbate is likely to be the limiting factor. There are data showing that K3 potentiates the cytotoxic/pro-oxidant properties of vitamin C when combined at a 1:100 ratio. The two can also be used intravenously in the same ratio.

Nettles Seed and Kidneys

For any patient with severely compromised kidney function and K+ levels over 6.0, it is wise to restrict green powders within supplements, and follow low potassium/magnesium diet (avoid magnesium supplements as well, as long as patient is not being dialyzed). Nettle seed tincture can help bring down creatinine and potassium over the next few months in many cases, after which the diet and supplement program can be liberalized in terms of potassium and magnesium content.

Egg Yolks as Material to Make Liposomal Botanical Preparations Just Before Consumption.

You can blend egg yolks with a number of botanical powders to make them into a liposomal form, keep in frig, and add to any beverage that they like, with gentle mixing. The phospholipids and cholesterol in egg yolks help to form a natural liposome which can increase the cellular uptake of the herbal compounds.

Herbal Compounds that inhibit mTOR/PI3K (phosphatidylinositol 3-kinase) and suppress cancer

Herbal Compound Herb (Botanical name)/ Type of cancer Reference

Curcumin Turmeric (*Curcumin longa*) Colon
Anticancer Res. 2009 August; 29(8): 3185–3190.

Numerous cancer cells
Cancer Res 2009;69(3):1000–8

Burkitt's lymphoma
J Pharmacol Sci. 2013;121(4):247–56

Prostate
Mol Cancer Ther. 2008 Sep;7(9):2609–20.

Leiomyosarcoma
Gynecol Oncol. 2011 Jul;122(1):141–8. Epub 2011 Mar 29.

Curcumin & EGCG Leiomyosarcoma
Int J Clin Oncol. 2012 Feb 15.

Green tea & Quercetin Prostate cancer
J Nutr Biochem. 2014 Jan;25(1):73–80.

EGCG (epigallocatechin gallate) Breast
Br J Cancer. 2008 Oct 7;99(7):1056–63. Epub 2008 Sep 16.

Baicalein Chinese skullcap (*Scutellaria b.*) Multiple cell lines
Biol. Pharm. Bull. 33(9) 1600–1604 (2010)

Wogonin Chinese skullcap (*Scutellaria b.*) Breast
Int Immunopharmacol. 2011 Dec 17.

Isoliquiritigenin Licorice (*Glycyrrhiza glabra* & other sp.)
Apoptosis. 2012 Jan;17(1):90–101.

Salidroside Rhodiola (*Rhodiola rosea*) Bladder
Mol Carcinog. 2011 Apr 22. doi: 10.1002/mc.20780.

Ursolic acid Sage (*Salvia off.*)/Holy basil Breast
Nutr Cancer. 2010;62(8):1074–86.

Withaferin-A Ashwagandha (*Withania somnifera*) Colon
Mol Cancer Ther. 2010 Jan ; 9(1): 202–210, *Invest New Drugs.* 2012 Nov 6.

Silibinin Milk thistle (*Silybum marianum*) Breast
Mol Cancer Ther. 2009 Jun;8(6):1606–12. Epub 2009 Jun 9.

Diosgenin Wild yam (*Dioscorea* spp) Breast
FEBS LETTERS, Volume 581, Issue 30, 22 December 2007, Pages 5735–5742

Forskolin Coleus forskolii cAMP activation
Cell Signal. 2011 December ; 23(12): 1927–1935.

Genistein Soy isoflavone Breast
Genome Med. 2010; 2(12): 90.

Fisetin Flavonoid in fruit (strawberries), Lung
Int J Cancer. 2012 April 1; 130(7): 1695–1705. *Lung Int J Cancer.* 2012 Apr 1;130(7):1695–705.

Resveratrol Phytoalexin from *Polygonum cuspidum* GBM - Brain
J Exp Ther Oncol. 2009;8(1):25–33.

Anti-inflammatory
J Biol Chem. 2012 Nov 2;287(45):38050–63. doi: 10.1074/jbc.M112.377028. Epub *Anti-inflammatory J Biol Chem.* 2012 Aug 30.

Sulforaphane ITC from Broccoli sprouts Anti-angiogenic
Oncol Rep. 2009 Dec;22(6):1473–8., *Oncol Rep.* 2009 Dec;22(6):1473–8., *Mol Luteolin Various fruits and vegetables Induces apoptosis in HT-2L9i mce ellts al. BMC Gastroenterology* 2012, 12:9

Danshen extract *Salvia miltiorrhiza* Cytoprotective
J Ethnopharmacol. 2012 Jan 31;139(2):541–8. doi: 10.1016/j.jep.2011.11.046.

Ginkgolide B Ginkgo biloba Inhibits atherosclerosis
PLoS One. 2012;7(5):e36237. doi: 10.1371/journal.pone.0036237. Epub 2012

Andrographolide *Andrographis* Breast cancer
Curr Mol Med. 2012 Sep;12(8):952–66.

Tocotrienols Breast cancer
Anticancer Agents Med Chem. 2012 Dec 11.

Reishi (*Ganoderma lucidum*) Breast cancer
PLoS One. 2013;8(2):e57431.

Anthracin *Anthriscus sylvestris* Breast cancer
Evid Based Complement Alternat Med. 2013;2013:385219. doi: 10.1155/2013/Prostate cancer Carcinogenesis. 2010 Aug;31(8):1424–33.

doi: 10.1093/carcin/bgg115. Epub 2010 Lung cancer
Int J Cancer. 2012 Apr 1;130(7):1695–705. doi: 10.1002/ijc.26178. Epub 2011

Nordihydroguaiaretic *Larrea divaricata* Breast cancer
Breast Cancer Res Treat. 2012 Nov;136(2):379–88. doi: 10.1007/s10549-012-2270

Cannabinoids *Cannabis sativa* Glioma cells
Cell Signal. 2005 Jan;17(1):25–37.

Salvianolic acid *Salvia miltiorrhiza* Retenia protective
Free Radic Biol Med. 2014 Jan 28

Dihydroartemisinin *Artemisia annua* Ovarian cancer
Biochemical and Biophysical Research Communications 444 (2014) 376–381

Apigenin Propolis and many plants Breast cancer
Toxicol Appl Pharmacol. 2008 Jan 15;226(2):178–91. Epub 2007 Sep 21.

Wortmannin Steroid metabolite of the fungi *Penicillium* efrunucleosum
Chem Biol Interact. 2006 Mar 25;160(2):123–33. Epub 2006 Feb 3

Pterostilbene *Pterocarpus marsupium* Colon cancer
Cancer Prev Res (Phila). Jul 2009; 2(7): 650–657.

Lycopene Tomatoes and other fruits & vegetables Prostate cancer;
Anticancer Agents Med Chem. 2014 May 21.

Carnosol *Rosemarinus officinalis* Leukemia
Cancer Lett. (2011), doi:10.1016/j.canlet.2011.02.005

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