

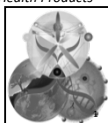
Herbs to Lift the Vital Spirit, Suppress Cancer and Reduce Reoccurrence and Metastasis

a symphony in harmony for cellular and spiritual reprogramming



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 Founder and Formulator, Natura Health Products

THE ECLECTIC TRIPHASIC
 MEDICAL SYSTEM (ETMS)



Four Main Reasons for Increased Rates of Cancer in America

- 1) **Woriment of the mind (stress)** - the move from low stress country life into high-stress city life
- 2) **Vaccinations** - induce immunological dysfunction & possibly mercury toxicity
- 3) **Diet** - overeating of meat and insufficient fruit and vegetables
- 4) **Abuse of stimulants** - alcohol, tobacco, drugs etc.

2015? No – Eli Jones in 1908

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Eli Jones Recommendation

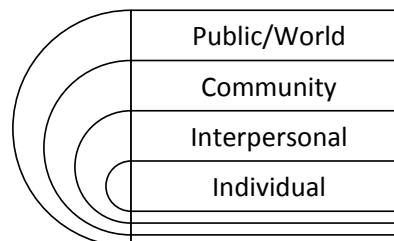
"In America we are becoming a nation of nervous, hysterical people. You must realize that if the nerve power falls below the normal standards there is danger of the invasion of cancer. What our people need to be taught is how to live. Good pure water, good pure air helps you make good healthy blood. Unadulterated food, mostly vegetables which are easily digested, keep the nervous system strong and vigorous. "STOP WORRYING and return to the simple way of life."

- Dr. Eli Jones 1908

A substantial amount of evidence shows an interaction between the CNS and the endocrine and immune systems

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Stress and the Physical Environment



The

levels.

All humans need to give and receive love, and feel a sense of belonging.

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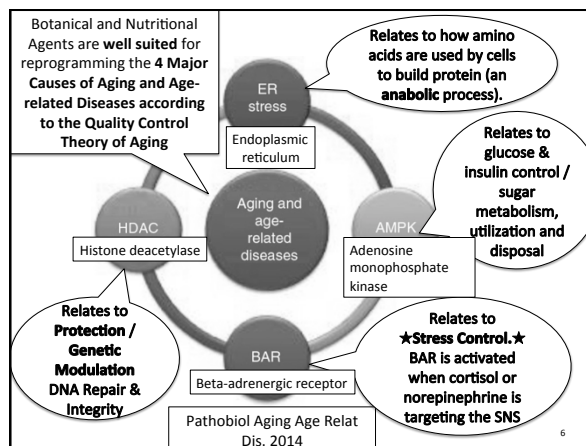
The Quality Control Theory (QCT) of Aging and Age Related Diseases

- 1) inadequate protein processing in a distressed endoplasmic reticulum (ER);
- 2) histone deacetylase (HDAC) processing of genomic histones and gene silencing;
- 3) suppressed AMPK (adenosine monophosphate kinase) nutrient sensing with inefficient energy utilization and excessive fat accumulation; and
- 4) **beta-adrenergic receptor (BAR) signaling and environmental and emotional stress.**

Reprogramming these systems to maintain efficiency would be a rational strategy for increasing lifespan and improving health.

Pathobiol Aging Age Relat Dis. 2014; 4: 10.3402/pba.v4.24835.

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What We Now Know

- Chronic behavioral stress results in higher levels of tissue catecholamines, greater tumor burden and more invasive growth of cancer.
- These effects are mediated primarily through activation of the tumor cell cyclic AMP (cAMP)-protein kinase A (PKA) signaling pathway primarily by the beta(2) adrenergic receptor (encoded by ADRB2).
- Tumors in stressed animals showed markedly increased vascularization and enhanced expression of tumor promoting growth factors – VEGF, MMP2 and MMP9.


Nat Med. 2006 Aug;12(8):939-44. Epub 2006 Jul 23; , 939 - 944 (2006)

β-adrenergic signaling (BAS)

- The β-adrenergic receptors (ADRBs) are part of the sympathetic nervous system, the general role of which is to ensure that the body responds fast and targeted upon danger, as well as to regulate energy expenditure.
- BAS appears to facilitate cancer progression and blockade of ADRBs may slow down tumor growth.
- Blockage of β-ARs significantly inhibit melanoma growth in mice by reducing tumor cell proliferation and activating tumor cell death. In addition, both drugs reduce tumor vascularization by inducing apoptosis of endothelial cells.
- ADRBs blockage inhibits inducible NO synthase (iNOS).

J Mol Med (Berl). 2013 Dec;91(12):1407-19; Naunyn Schmiedebergs Arch Pharmacol. 2014 Jun;387(6):533-43.

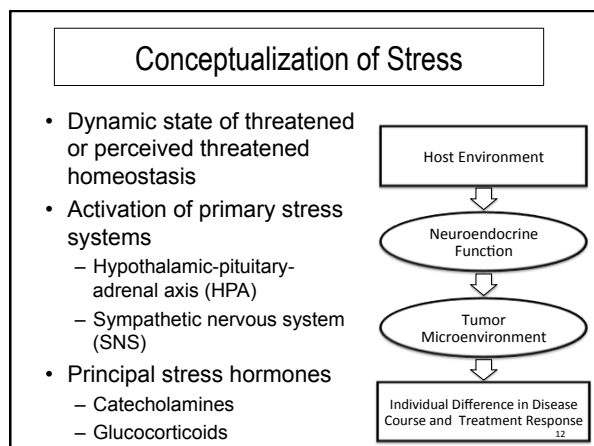
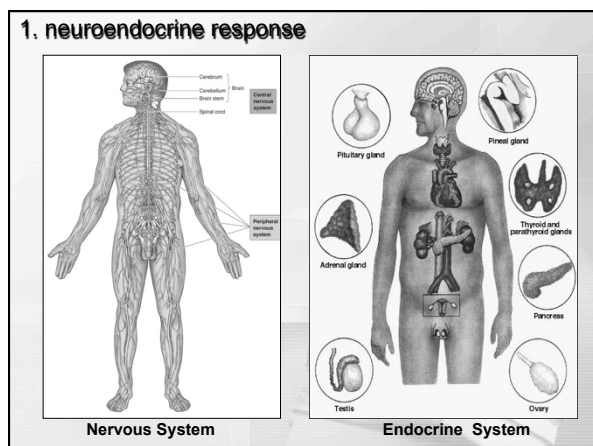
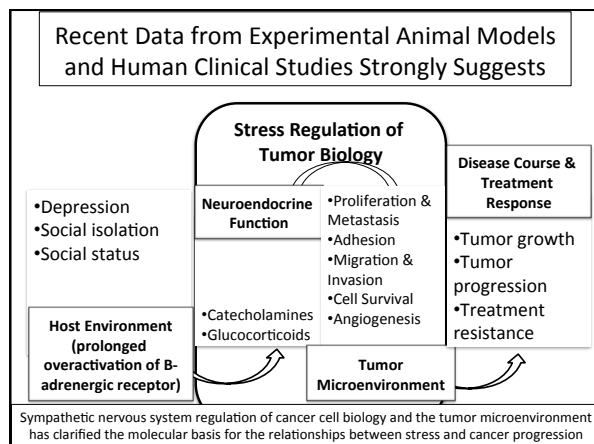
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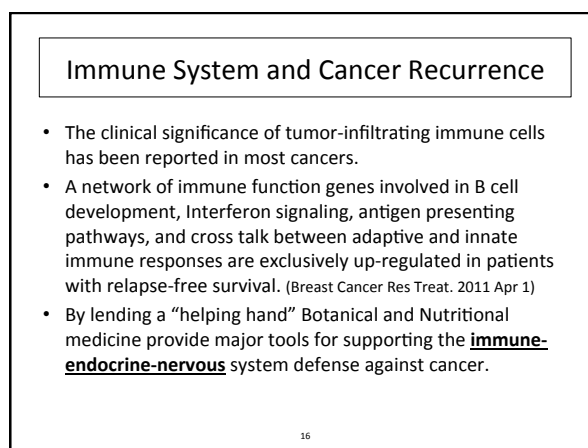
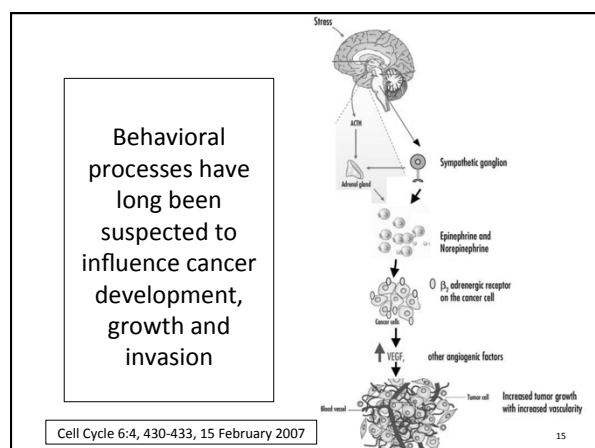
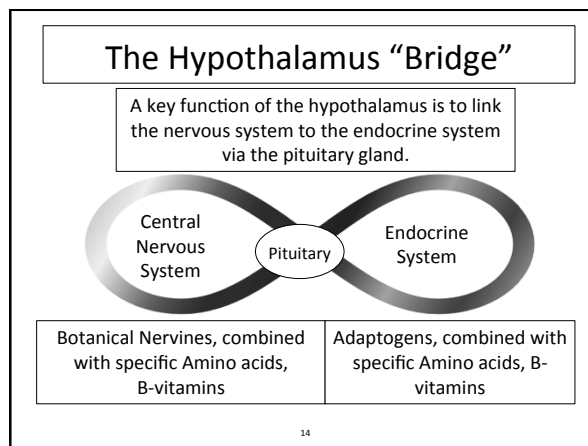
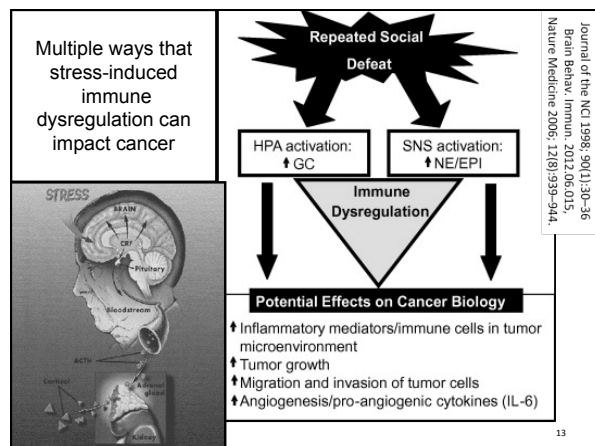


"Flight and Fight" Response Linked with Cancer

- Considerable support exists for suspecting stress-induced tumor growth and cancer progression via an alteration of immunological, neurochemical, and endocrinological function.
- β -blockers use in patients with cancer is now associated with reduced metastasis and cancer reoccurrence.
- Recently a study confirmed that Beta-blocker use is associated with a reduced risk of melanoma recurrence and death.
- β -blocker use in triple-negative breast cancer (BC) in postmenopausal women (800/11 years) was associated with a significantly decreased risk of BC-related recurrence, metastasis, and BC death.

Mayo Clinic Proceeding November 2013 Vol. 88 # 11; Mayo Clin Proc. 2013;88(11):1196-1203; Breast Cancer Research and Treatment, August 2013, Volume 140, Issue 3, pp 567-575





Negative Effects of Chronic Stress

- **Psychologic – depression, anxiety** ←
- Heart disease – vessel constriction, rhythm disturbance, blood clots, increased cholesterol, increased blood pressure
- Stroke
- Susceptibility to infections
- **Cancer progression** ←
- Gastrointestinal: Irritable Bowel Syndrome, peptic ulcers, inflammatory bowel disease; eating problems (weight gain or loss, anorexia, bulimin)
- Diabetes
- Pain
- Sleep disturbances

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Psychoneuroimmunology

- A field of medical research that studies the relationships between the nervous, endocrine and immune systems.
- Stress changes the normal balance and functioning of the immune system.
- An **adequate balance** between **catabolic** (mobilization of energy) and **anabolic** processes (growth, healing) is considered necessary for long-term health and survival.
- In modern society, which is characterized by a rapid pace of life, high demands, efficiency and competitiveness, it is likely that lack of rest, recovery and restitution is a greater health problem than the absolute level of stress.

Psychoneuroendocrinology. 2005 Jun 14 18

Psychosocial Risk Factors and Cancer Progression

1. In 330 studies, stress-related psychosocial factors were associated with poorer cancer survival ($P < 0.001$)
2. Largest survival effects documented for:

• Hepatobiliary cancer	1.88 (1.07-3.30)
• Head and neck cancer	1.58 (1.22-2.03)
• Lymphoid or hematopoietic cancer	1.32 (1.11-1.56)
• Lung cancer	1.17 (1.03-1.34)
• Breast cancer	1.13 (1.05-1.21)
3. In 53 studies, stress-related psychosocial factors were associated with higher cancer mortality ($P < 0.001$)

Chida et al. (2008) *Nature Clinical Practice Oncology*

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Psychological State and Disease Outcome

Depression as well as anxiety and cancer commonly occur together. The prevalence of depression and anxiety amongst cancer patients increases with disease severity and symptoms such as pain and fatigue.



Biological Psychiatry, Volume 54, Issue 3, 1 August 2003, Pages 269–282

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Depression and Anxiety in Cancer Patients

- Is a major public health problem and has an especially large effect on health when comorbid with a chronic medical condition.
- According to a recent 2015 study 38% cancer patients demonstrate depressive symptoms.
- Clinicians working in cancer services have recognized that depression is often undiagnosed and untreated and that these shortcomings in care can have substantial effects on patients' quality of life.
- Targeting the Vital Spirit with botanical medicine, together with stress and behavior modification, has a significant positive effect on reducing depression and anxiety.

Br J Psychiatry 2004; 184: 386–392; Br J Psychiatry 2004; 184: 386–392; Lancet 2000; 356(9238): 1326–1327; Br J Cancer 2004; 90(2): 314–320; Br J Cancer 2001; 84(8): 1011–1015; BMJ Support Palliat Care. 2015 Feb 9.

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Depression in Cancer Patients

- Although this normal grief response is expected to resolve in the first 2 weeks after diagnosis, many cancer patients eventually suffer from clinically diagnosable depression.
- Heightened depression is not limited to the active treatment period and may persist for months or even years after successful cancer treatment
- Depression aggravates weight loss in head and neck cancer patients and significantly reduces Q-o-L - Depressive patients were affected more by radiotherapy with respect to weight loss compared to non-depressive patients.
- Twofold increase in breast cancer risk after separation, divorce, or death of spouse (n > 10,000).

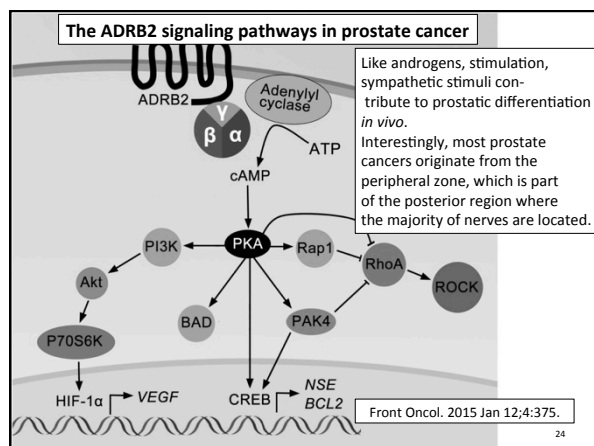
Primary Care: Clinics in Office Practice Vol 36, Issue 4, Dec 2009, Pages 703–719; Gen Hosp Psychiatry. 2014 Sep 6. pii: S0163-8343(14)00216-3; Lillburg et al., 2003

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Stress, Lack of Social Support Linked to Prostate Cancer Mortality

- During a mean follow-up of 51.3 months after the questionnaires were returned, there were 127 prostate cancer deaths (3.1%) and 276 deaths from other causes (6.7%).
- Men in the highest tertile of perceived stress had a 66% increased risk of prostate cancer-specific mortality compared to men in the lowest tertile.
- A sensitivity analysis was performed to ensure that this finding was not biased by rapidly deteriorating health and/or hastened mortality.
- After excluding men who died of prostate cancer within six months of responding to the questionnaire, the result did not change.

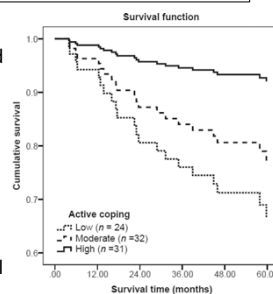
Stress, Lack of Social Support Linked to Prostate Cancer Mortality. Medscape. Feb 24, 2014.



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Protective Role of Social Support in Mortality Outcomes

- Greater use of active coping prior to surgery for suspected endometrial cancer is associated with lower probability of all-cause mortality 4-5 years post-surgery.
- Psychosocial-survival relationship exists independent of biobehavioral factors.



Br J Health Psychol. 2014 Nov;19(4):737-50. doi: 10.1111/bjhp.12070.

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Stress effects on ovarian carcinoma growth *in vivo*

- Enhanced tumor growth and progression
- Two molecular mechanisms identified:
 1. Stress regulation:
 - Catecholamine signaling *via* beta-adrenergic receptors
 - Depletion of dopamine
 2. Tumor biology:
 - Up-regulated angiogenesis

Within the tumor microenvironment, β -adrenergic receptors on tumor and stromal cells are activated by catecholamines from local sympathetic nerve fibers (norepinephrine) and circulating blood (epinephrine). Tumor-associated macrophages are emerging as key targets of β -adrenergic regulation in several cancer contexts.

Clin Cancer Res. 2012 March 1; 18(5): 1201-1206. doi:10.1158/1078-0432.CCR-11-0641.

Stress • Immune Dysfunction • Cancer

- Stress hormones regulate a panel of important physiological functions and disease states including cancer.
- Cancer patients have increased levels of stress hormones.
- Stress-induced immune dysregulation results in significant health consequences for immune related disorders including viral infections, chronic autoimmune disease, and tumor growth and metastasis.
- The beta2-adrenergic receptor (ADRB2) is the most involved in the carcinogenic processes.
- ADRB2 stimulates multiple signals involved in cancer growth, angiogenesis and invasion.

Journal of the National Cancer Institute 1998; 90(1):30-36 Behav. Immun. (2012),
<http://dx.doi.org/10.1016/j.bbi.2012.06.015>, Nature Medicine 2006; 12(8):939-944.
 Oncol Res. 2010;19(1):45-54; Semin Cancer Biol. 2013 Dec;23(6 Pt B):533-42. 27

Cortisol down-regulates the expression of the breast cancer susceptibility gene BRCA1 in the nonmalignant mouse mammary cell line EPH4.

- This effect is concentration-dependent, is reliant on the continuous presence of cortisol, and is not affected by the addition of lactogenic hormones, or growth conditions.
- Cortisol was also found to negate a known positive effect of estrogen on BRCA1 expression and, therefore, may interfere with estrogen-related signaling in mammary epithelial cells.
- Because BRCA1 activity is important for a number of intracellular pathways involved in prevention of tumorigenesis, its observed down-regulation may represent a novel molecular mechanism for cortisol's involvement in breast cancer development.

Genes Chromosomes Cancer. 2008 Apr;47(4):341-52. doi: 10.1002/gcc.20538. 28

Adrenergic Signaling Promotes Angiogenesis through Endothelial Cell-Tumor cell Crosstalk

- The neurotransmitter norepinephrine upregulates VEGF expression in breast cancer cells.
- The effects of norepinephrine were further enhanced when the endothelial cells were co-cultured with breast cancer cells.
- Prevention of Skin Carcinogenesis: Both topical and oral Carvedilol (β -Blocker) inhibited DMBA-induced epidermal hyperplasia ($P < 0.05$) and reduced H-ras mutations.
- Carvedilol inhibited EGF-mediated activator protein-1 (AP-1) activation.

Endocr Relat Cancer. 2014 Oct;21(5):783-95; Cancer Prev Res (Phila). 2014 Nov 3.

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Norepinephrine Promotes Tumor Microenvironment Reactivity during Melanoma Progression

- β 3-AR can (1) instruct melanoma cells to respond to environmental stimuli, (2) enhance melanoma cells response to stromal fibroblasts and macrophages, (3) increase melanoma cell motility and (4) induce stem-like traits.
- Noteworthy, β 3-AR activation in melanoma accessory cells drives stromal reactivity by inducing pro-inflammatory cytokines secretion and *de novo* angiogenesis, sustaining tumor growth and melanoma aggressiveness.
- β 3-ARs also play a mandatory role in the recruitment to tumor sites of circulating stromal cells precursors, in the differentiation of these cells towards different lineages, further favoring tumor inflammation, angiogenesis and ultimately melanoma malignancy.

www.impactjournals.com/oncotarget, December 06, 2014

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Chronic Stress Induces Chronic Inflammation

- Chronic stress induces changes in sensitivity of inflammatory pathways to the signals of multiple stress systems
- Emerging evidence suggests that stress-related changes in the sensitivity of target systems toward glucocorticoid regulation, might help explain inflammatory disinhibition and development of disease related to inflammation.
- It is the autonomic nervous system that also plays an important role in the regulatory control of the inflammatory cascade.
- Chronic stress can increase pro-inflammatory pathways which in turn ignite and/or induce cancer angiogenesis, invasion and recurrence.

Psychoneuroendocrinology. 2012 Mar;37(3):307-16;
Zhong Xi Yi Jie He Xue Bao. 2010 Nov;8(11):1006-13;

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Cancer and your Immune System

- The marvel of your immune system is its ability to distinguish between what's 'you' and belongs from what's 'new' and doesn't belong.
- Antigen
 - Any 'new' substance that triggers your immune response
- Cancer Fighters
 - IFs, IL-2 & 12, NK cells, Cytotoxic and T-Lymphocytes
- Stress redirects and prioritizes our internal energy immune adaptive and cancer inhibiting capability.
- Chronic stress has been shown to cause decreased immunity, leading to hyper-inflammatory (TH2) states (autoimmune conditions), poor production of NK cells and diminished cytotoxic T-cell response, an overall decreased cytotoxicity in cancer patients.

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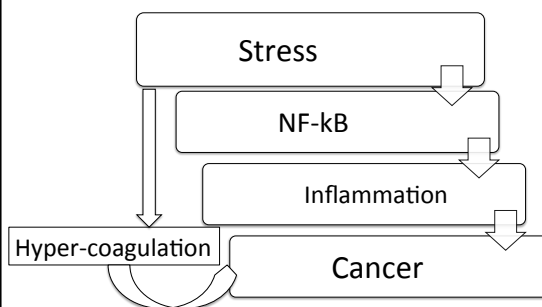
Chronic Dysfunctional Response to Stress

- Can induce systemic platelet activation (a hypercoagulable state).
- Acute stress includes release of epinephrine by the adrenal medulla. Epinephrine activates platelets by binding to alpha-2A adrenergic receptors.
- **Hypercoagulability** could be targeted by monoclonal antibodies directed against the platelet-specific alpha-2 adrenergic receptor.
- Better yet, Herbal medicine directed at nourishment to the Vital Spirit, Liver, Kidney and Circulatory systems.

Medical Hypotheses (2005) 65, 542–545; Med Hypotheses. 2006;67(5):1065-71. Epub 2006 Jun 6.

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One Transitional Way to Cancer



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Catecholamine-Induced β 2-adrenergic Receptor (β 2-AR) Activation Leads to Herceptin Resistance

- Correlation of β 2-AR level with Her2 status was demonstrated in breast cancer tissue
- Catecholamine stimulates Her2 mRNA expression and promoter activity.
- The antitumor activities of herceptin (trastuzumab) were significantly impeded by chronic catecholamine stimulation in gastric cancer cells and in the mice bearing human gastric cancer xenografts.
- β 2-AR expression induced by epinephrine upregulates MUC4 leading to the activation STAT3 and ERK.

J Immunol. 2013 Jun 1;190(11):5600-8; Breast Cancer Res Treat. 2011 Jan;125(2):351-62.

β -Adrenergic Receptors (BAR) Promote the Metastatic Phenotype in Breast Cancer Cells

- Rap1B is a small GTPase that suppresses the metastasis of breast cancer cells by increasing cell-cell adhesion
- In breast cancer, a decrease in Rap1B prenylation and subsequent loss of Rap1B at the plasma membrane decreases cell-cell adhesion and increases cell scattering, which promotes the metastatic phenotype.
- Targeting of G protein-coupled receptors, especially those such as the β AR, to increase cell adhesion and decrease cell scattering could provide a promising therapeutic approach to reduce breast cancer metastasis.

Cancer Biol Ther. 2015 Jul 24:0.

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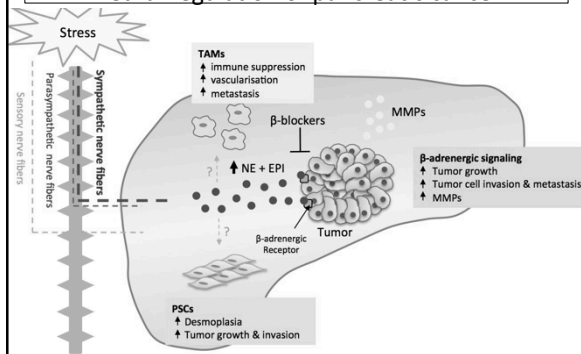
Chronic stress and Pancreatic cancer

- Chronic stress plays as a physiological regulator of neural-tumor interactions in driving the progression of pancreatic cancer.
- These studies propose several approaches to target stress signaling via the β -adrenergic signaling pathway in order to slow pancreatic tumor growth and metastasis.
- They also provide evidence to support the use of β -blockers as a novel therapeutic intervention to complement current clinical strategies to improve cancer outcome in patients with pancreatic cancer.

Brain Behav Immun. 2014 Aug;40:40-7, Cancers (Basel). 2015 Jul 17;7(3):1292-312.

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Neural regulation of pancreatic cancer



Cancers (Basel). 2015 Jul 17;7(3):1292-312.

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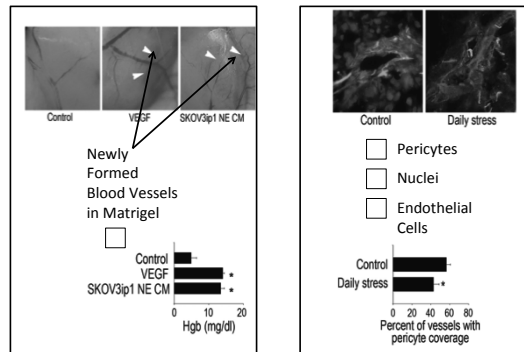
VEGF Levels and Social Support in Patients with Ovarian Cancer

- Women with ovarian carcinoma who reported higher levels of social well being had lower levels of VEGF ($P = 0.005$).
- Greater support from friends and neighbors ($P = 0.005$) and less distance from friends ($P = 0.04$) were facets of social well being that were associated with lower VEGF levels.
- These findings suggest a possible mechanism by which poor social support may be associated with disease progression.

Cancer. 2002 Aug 15;95(4):808-15.

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Effects of Chronic Stress on Angiogenesis



Antoni et al., Nature Reviews Cancer, 2006, Thaker et al., 2006

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Antiproliferative effects of β -blockers on human colorectal cancer cells

- Adrenergic activation plays an important role in colon cancer cell proliferation, most probably through β -AR.
- The β -blockers under study were able to reverse the proliferation induced by α - and β -adrenergic receptors and catecholamines, and some of these blockers significantly decreased the proliferation of HT-29 cells.

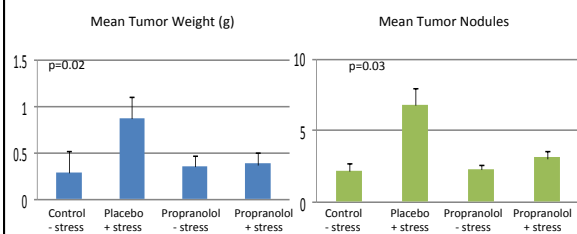
Oncol Rep. 2015 May;33(5):2513-20. doi: 10.3892/or.2015.3874. Epub 2015 Mar 23.

β -Blockers, a New Opportunity for Conventional Drugs

- Propranolol has shown to significantly reduce the primary tumor development, nodal/metastatic occurrence and breast cancer-specific mortality.
- β -blockers significantly improved the relapse-free survival in all patients with breast cancer.
- **Natural compounds**, whole herbal extracts, and life-style interventions are effective modulators.
- Example: **Quercetin** inhibits noradrenaline-promoted invasion of human breast cancer cells **by blocking β -adrenergic signaling**.

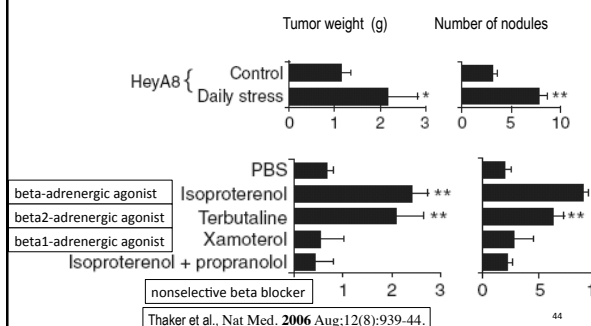
Seminars in Cancer Biology 23P (2013) 533–542; Oncotarget 2010;1:628–38; J Clin Oncol 2011;29:2635–44; Arch Biochem Biophys. 2014 Sep 1;557:18-27

Propranolol, a nonselective beta blocker, counteracts the effects of chronic stress on tumor growth



Adapted from Thaker et al., (2006)

Exposure to chronic stress & the benefit of a B-blocker *in vivo* ovarian carcinoma growth



β -adrenergic receptors (BAR) and Melanoma growth and metastasis

- Stress has an emerging role in cancer and targeting stress-related BAR has been proposed as a potential therapeutic approach in melanoma.
- β 3-AR can (i) instruct melanoma cells to respond to environmental stimuli, (ii) enhance melanoma cells response to stromal fibroblasts and macrophages, (iii) increase melanoma cell motility and (iv) induce stem-like traits.
- Selective β 3-AR antagonists act as potential anti-metastatic agents against melanoma growth and metastasis.

Oncotarget. 2015 Mar 10;6(7):4615-32.

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How Can Surgery Promote Cancer Metastasis?

"A surgeon can only cut out what is seen and felt under the knife, while millions of cancer cells grow and multiply in the blood, the nuclei of future cancer. Another fact that the surgeon forgets is that every operation is a shock to the nervous system, it lowers the nerve power, weakens the power of resistance to disease and thus encourages the invasion of cancer."

Eli Jones (1894)

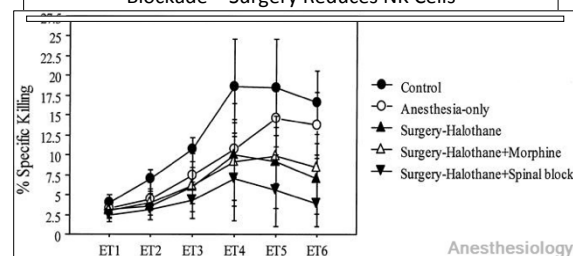
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Surgical Stress is Immune-suppressive causing a sharp decline in Natural killer (NK) Cells

- Stress-induced suppression of NK cells is sufficient to cause enhanced tumor development. Cancer 1992; 70: 2192-202, Int J Cancer 1999; 80: 880-8
- Surgical stress compromises host resistance to infectious and malignant diseases in both experimental and clinical settings. Acta Anaesthesiol Scand 1992; 36: 201-20
- There direct in vivo evidence that surgical stress impairs global NK cell function. Surgical stress promotes the development of cancer metastases by a coagulation-dependent mechanism involving NK cells Ann Surg. 2013 Jul;258(1):158-68.
- Perioperative therapies aimed at enhancing NK cell function will reduce metastatic recurrence and improve survival in surgical cancer patients. Cancer Res. 2013 Jan 1;73(1):97-107.

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The Tumor-promoting Effect of Surgery by Spinal Blockade – Surgery Reduces NK Cells



Effects of anesthesia and surgery on natural killer (NK) cytotoxic activity (expressed as percent specific killing at six effector-to-target [ET] ratios), assessed 5 h after the beginning of surgery. Surgery suppressed NK activity compared with the control group, with no significant difference between the various anesthetic regimens.

Wolters Kluwer | Lippincott Williams & Wilkins

Anesthesiology. 94(6):1066-1073, June 2001.

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Surgical stress increases lung tumor metastases by impairing NK cells.



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Surgery and Immunosuppression

A history of stressful or traumatic life events may reduce host resistance to tumor growth and turn on the metastatic cancer switch.

These findings are consistent with a possible long-lasting effect of previous life stress on stress response systems such as the hypothalamic-pituitary-adrenal (HPA) axis.

Journal of Psychosomatic Research
Volume 63, Issue 3, September 2007, Pages 233-239

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Part 2: the ETMS Approach to Stress, Anxiety, and Cancer Inhibition

Botanical medicine is the soul of the ETMS, it permeates and is integrated into all its applications.

“For the earth which drinks in the rain that comes often upon it, *and* brings forth **plants** fit for them by whom it is cultivated, receives **blessing from God**” Hebrews 6:7

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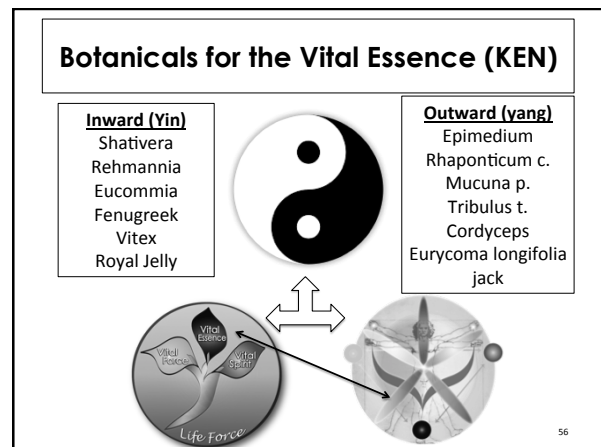
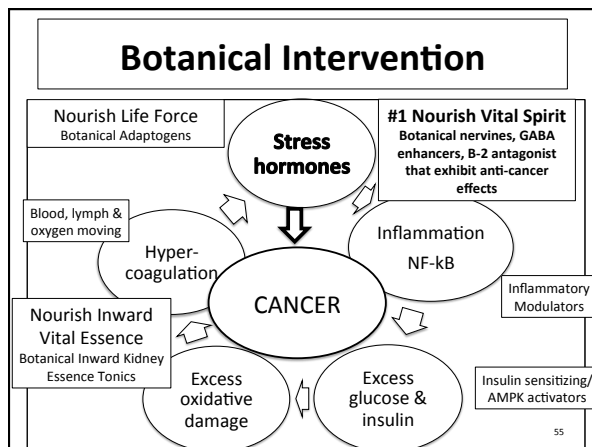
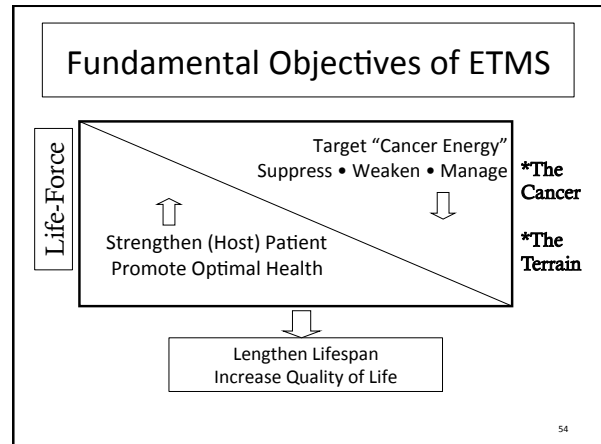
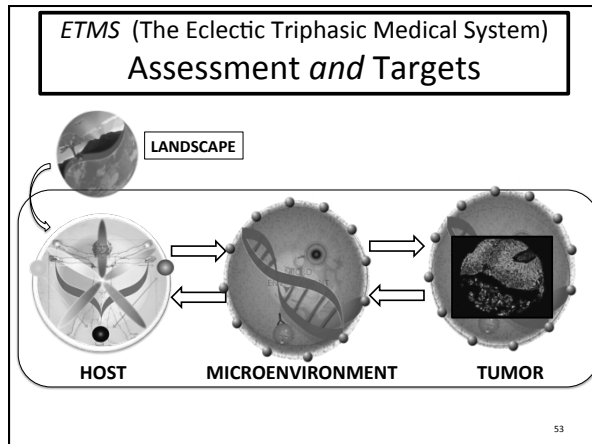
Nature/Gaia provides for us the healing plants, but they are humble.

- Praise be you my Lord,
for our sister Mother Earth,
who nourishes and sustains us all,
and brings forth divers fruits,
with many – colored flowers
and herbs.

– St. Francis of Assisi



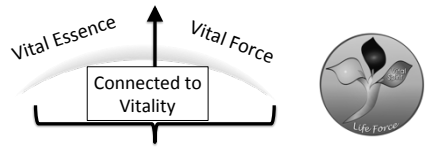
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Vital Spirit

our consciousness, mental health, and our "presence".

Rising Vital Spirit = Pilgrimage of Life



Constantly in flux: energy in -- energy out

"the fruit of the Spirit is love, joy, peace, long-suffering, gentleness, goodness, faith, meekness, temperance: against such there is no law." (Gal. 5:22, 23)

The Supportive Roles of Theology and Spirituality

- A literature review of the supportive roles of religion and spirituality (R/S) in end-of-life (Eula) and palliative care of patients with cancer in a culturally diverse context.
- Examined 26 noteworthy articles published between August 2013 and August 2014 from five well supported databases.
- Concluded R/S provide the individual and their families with a practical context and social memory, which includes traditions and social family practices for maintaining meaning and well-being.

Curr Opin Support Palliat Care. 2015 Jan 12.

Contemplate/Mediate Lectio divina

- A VERY ANCIENT art practiced by all Monks - a slow, contemplative praying of the Scriptures or other great spiritual writings as a means of union with God.
- It begins with cultivating the ability to listen deeply, to hear "with the ear of our hearts."
- We should allow ourselves to become women and men who are able to listen for the still, small voice of God (**I Kings 19:12**), the "faint murmuring sound" which is God's voice touching our hearts and speaking to us.
- We are listening for the still, small voice of God that will speak to us personally - not loudly, but intimately.
- **Read Pope Francis on the 'Great Mystery'**
- After you apply the Clinical Thinking then pray as a means to both form a protocol and the words you speak to your patient.

'Oil of Anointment'

A blend of sacred essential oils for blessing, healing, and protection

Dosage & Directions:

- Massaged small amount to any area/ organs of the body that need healing; as well as the hands, feet, &/or forehead with prayers & sacred intent

- **Ingredient(s)**
- EO Sacred Frankincense
- Hypericum (St. John's wort) Oil
- EO true Lavender
- EO Spikenard
- EO Holy Basil
- EO Myrrh
- EO Sandlewood
- EO Rose
- EO Nutmeg
- DMSO

Patient Optimism and Mastery—Do They Play a Role in Cancer Patients' Management of Pain and Fatigue?

- Patients who are more optimistic, suffered from fewer comorbid conditions, including less severe pain and lower fatigue severity scores.
- Clinicians involved in the care of cancer patients should recognize, encourage, promote, and take advantage of these traits in their patients to help them more effectively manage their cancer care, so that they ultimately can achieve a better quality of life during the sequel of the cancer experience.

Journal of Pain and Symptom Management Volume 36, Issue 1, July 2008, Pages 1–10

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Personality, Disease, and Stress

- People who only see negative aspects of a stressor may be more vulnerable to stress than those who make more positive appraisals of the situation.
- People who are less vulnerable to stress have personalities that act as buffers.
- These individuals generally have more positive outlooks on life.
- Cancer patients with optimistic outlooks and a healthy “Vital Spirit” tend to survive longer than cancer patients without these characteristics.

Integr Cancer Ther. 2014 Mar 9;13(4):301-309;

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Example of Herbs that Enhance Vital Spirit Reduce Anxiety & Suppress Cancer

Herb	Active compounds
St. John's wort (<i>Hypericum perforatum</i>)	Hyperforin, and the hypercines
Rauwolfia (<i>Rauwolfia serpentina</i> or <i>vomitoria</i>)	Reserpine & more - depletes catecholamines from peripheral sympathetic nerve endings
Passion flower (<i>Passiflora incarnata</i>)	Apigenin, luteolin, chlorogenic acid and chrysin
Albizzia (<i>Albizzia julibrissin</i>)	Triterpenoid saponins - julibroside J28
Ziziphus (<i>Ziziphus spinosa</i>) seed	Protojubilogenin type triterpene bisdesmosides, protojubilosides A, B, and B1
Kava Kava (<i>Piper methysticum</i>)	Kavalactones - flavokawain B

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St. John's wort (*Hypericum perforatum*)

Has been used in herbal medicine for centuries. “Neurological adaptogen” and stress-reliever/protector.

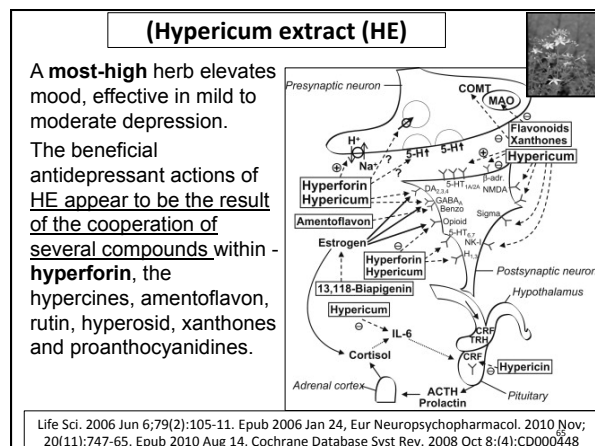
It is a neurological restorative plant that repairs nerve tissue damage and is among the best-suited agents available.

Profound antidepressant-like activity of adhyperforin, a novel constituent of *Hypericum perforatum* L.

Arch Pharmacol. 2011 Apr;383(4):415-22. Epub 2011 Feb 19. BMC Complementary and Alternative Medicine 2011, 11:7; Eur J Pharm Biopharm. 2003 Jul;56(1):121-32. Clin Cancer Res. 1996 May;2(5):843-6. Oncol Res. 2000;12(9-10):409-18. PLoS One. 2010 Mar 9;5(3):e9558. Int J Cancer. 2009 Jul 1;125(1):34-42; Tian, J., Zhang, F., Cheng, J., Guo, S., Liu, P., & Wang, H. (2014). Antidepressant-like activity of adhyperforin, a novel constituent of *Hypericum perforatum* L. *Reports*, 4, 5632. doi:10.1038/srep05632

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Hypericum extract (HE) clinical studies in Oncology

- Significantly inhibited tumor growth in tumor-bearing animals.
- In one animal study involving prostate cancer treatment with HE inhibited tumor growth by 70%. Regional lymph node metastasis was observed in 100% of the controls mice compared to 30% of mice treated with HE.
- Profound anti-angiogenic effects
- Is a potent radiosensitizer as well
- HE decreased blood levels of certain chemo drugs (CPT-11), but does not reduce effectiveness, and actually protects & potentiates.

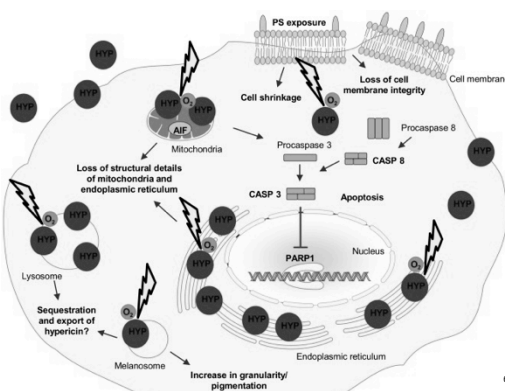
Chemico-Biological Interactions (2010), doi:10.1016/j.cbi.2011.02.026
 Cancer Letters 210 (2004) 27–33; Int J Cancer. 2005 Dec 10;117(5):775-80
 Clin Cancer Res. 1996 May;2(5):843-6; Pharm Res. 2005 Jun;22(6):902-14. Epub 2005 Jun 8
 Toxicol Appl Pharmacol. 2007 Apr 1;220(1):108; author reply 109-10

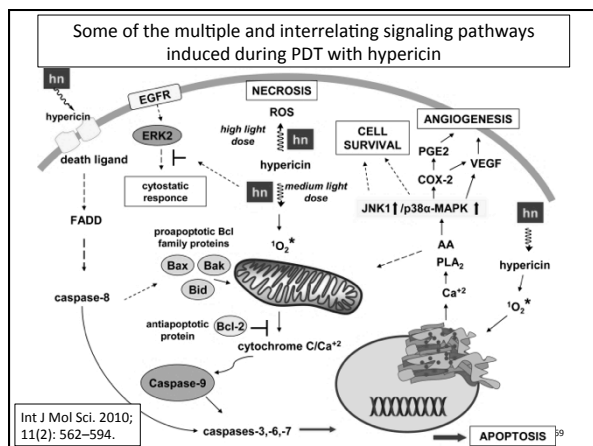
Downregulation of β adrenergic receptors in rat C6 glioblastoma cells by hyperforin and hyperoside from St John's wort.

- Hyperforin and hyperoside reduce β 2-adrenergic sensitivity in C6 cells, emphasizing the potential usefulness of St. John's Wort dry extracts in clinical treatment of depressive symptoms.¹
- The treatment of C6 glioblastoma cells with hyperforin and hyperoside results in a reduced β 1 AR density in the plasma membrane and a subsequent reduced downstream signaling.²
- Hypericin-Photodynamic Therapy Induces metastatic Melanoma cell death³
- NOTE: I often dose higher and higher until I see a photosensitive response

Biochemistry. 2007 May 1;46(17):5106-13; Mol Clin Oncol. 2013 Mar;1(2):395-399; PLoS One. 2014; 9(7): e103762.

Melanoma response mechanisms to hypericin-PDT





Hypericin naphthodianthrone from Hypericum

- Produces a potent and irreversible inhibition of the epidermal growth factor (EGF) receptor tyrosine kinase activity.
- Although hypericin inhibits EGF signaling, it does not appear to act specifically on the EGF-R (MEK).
- Hypericum also inhibits HER2 neu signaling as well.
- Hypericin inhibited the glioma growth in a dose-related manner, with a marked inhibition of growth in the low-micromolar concentration range.

Biochemical Pharmacology, Vol. 46, No. 11, pp. 1929-1936, 1993; pathway. Anticancer Res. 2001 Jul-Aug;21(4A):2649-55; Anticancer Res. 2001 Jul-Aug;21(4A):2649-55. Neurosurgery, October 1994 - Volume 35 - Issue 4 - p 705-710.

Kava (*Piper methysticum*)

- Cultivated in the South Pacific for over 3,000 years
- The most important cultivated plant from a social perspective in the history of Pacific island societies.
- Traditional kava preparation made from the roots are used for three different types of ceremony:
 - (1) for very formal occasions such as to honor royalty,
 - (2) ceremonies performed at community meetings,
 - (3) informal kava ceremonies, such as for a social occasion.
- Kava root extracts and the active components kavalactones and flavokawains suppress cancer
- Even though they smoke, there is a low incidence of cancer (lung)



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Kava Actions



NOTE: Nicotine-induced activation of the noradrenaline-initiated signaling cascade and deficiency in inhibitory GABA, in the nicotine-addicted brain, may contribute to the development of NSCLC in smokers.

PLoS ONE, Jan. 1012, Issue 1 29915

Unusually low cancer incidences (men especially) in the Pacific Island nations despite a high portion of smokers in these populations ? Kava drinking

Anti-anxiety

Anti-inflammatory

Anti-tumor

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Kava Kava (*Piper Methysticum*)

- Very effective anxiolytic activity that creates a heightened sense of well-being and contentment
- Useful in the treatment of anxiety, insomnia, nervous disorders
- Aids people in withdrawing from anti-anxiety drugs
- Anti-inflammatory evidenced by its inhibition of TNF-alpha and NF-kB -- over-activated in PD
- Caution should be taken when combining it with L-dopa and/or benzodiazepines
 - Start with small doses in combination with nervines and adaptogens
 - Kava fluid extract as 10-20% of formulation is safe and effective for people with PD and anxiety

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Kavalactones and the endocannabinoid system: yangonin is a novel CB₁ receptor ligand.

- Cannabinoid receptor ligands share pharmacological properties with kavapyrones.
- Yangonin exhibited affinity for the human recombinant CB₁ receptor with a K_i=0.72 μM and selectivity vs. the CB₂ receptor (i)₅₀>10 μM).
- The CB₁ receptor affinity of yangonin suggests that the endocannabinoid system might contribute to the complex human psychopharmacology of the traditional kava drink and the anxiolytic preparations obtained from the kava plant.

Pharmacol Res. 2012 Aug;66(2):163-9.

74

Kava extract anti-tumor actions

Type of cancer	Mechanism	Reference
Significantly inhibits 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) and benzo(a)pyrene (BaP)-induced lung tumorigenesis in A/J mice	Increase in caspase-3 & inhibited NF-kB	Am J Chin Med. 2011;39(4):727-42.
Inhibits the growth of p53 defective bladder cancer in mice	Decreased expression of Ki67, survivin and XIAP and increased expression of p27	Cancer Prev Res (Phila). 2013 Oct 11.
Induces cell cycle arrest in several cancer cell lines	Increases the ratio of Bax/Bcl-xl; increased the amount of p21 & p27 cell cycle regulatory proteins	Cancer Cell International 2013, 13:102; J Agric Food Chem 2009, 57:6.
Inhibits growth of human osteosarcoma cells	G2/M cell cycle arrest and apoptosis	www.ncbi.nlm.nih.gov/pmc/articles/PMC3681603/
Reduce colon cancer risk in animals	Prevents dimethylhydrazine induced colon carcinogen	Nutr Cancer. 2012 Aug;64(6):838-46.

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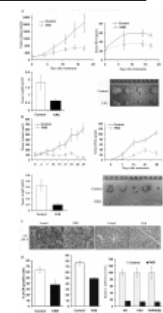
Kava extract anti-tumor actions

Type of cancer	Mechanism	Reference
Inhibits the growth of bladder tumor cells in a nude mice model (57% of inhibition)	Strong antiproliferative and apoptotic effect. Decreases Bcl-2	Cancer Res 2005; 65: (8). April 15, 2005
Reduce tumor growth, AR expression in tumor tissues and levels of serum PSA in mice in prostate cancer	Down-regulated the expression of both the full-length AR and AR splice variants	Cancer Prev Res (Phila). 2013 Oct 11.
Exhibits robust apoptotic effects and induces G2/M arrest of a uterine leiomyosarcoma cell line.	Note: Acted synergistically when combined with docetaxel and gemcitabine	J Obstet Gynaecol Res. 2012 Aug; 38(8):1086-94
Inhibited tobacco induced lung tumorigenesis in A/J mice	Kavalactone-enriched fraction B fully recapitulated kava's chemopreventive efficacy	Cancer Prev Res (Phila). 2014 Jan; 7(1):86-96.

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Kava root extract and FKB inhibited tumor growth, reduced serum PSA levels and decrease AR expression in tumor tissues in patient-derived PCa xenograft models.

- Kava extract and flavokawain B effectively down-regulated the expression of both the full-length AR and AR splice variants.
- The kava extract and kavalactones accelerated AR protein degradation, while flavokawain B inhibited AR mRNA transcription via decreasing Sp1 expression and the binding of Sp1 to the AR promoter.
- The kava root extract and flavokawain B reduce tumor growth, AR expression in tumor tissues and levels of serum PSA in the patient-derived PCa xenograft models.



PLoS One. 2012; 7(2):e91213.

Rauwolfia vomitoria and *serpetina*

- Traditionally used to treat hypertension, anxiety, insomnia, and insanity.
- Contains at least 40 actives alkaloids of which the most noted is Reserpine - an old drug used to treat hypertension.
- Interferes with the function of the sympathetic nervous system, reducing catecholamines from peripheral sympathetic nerve ending. Planta Medica 1977 Aug;32(1):88-99
- Rauwolfia is useful for Psychosis/OCD Br Med J. 1955 Nov 5; 2(4948): 1121–1122; *J Ment Sci.* 1957 Jul;103(432):464-74.
- Anti-prostate cancer activity of a beta-carboline alkaloid enriched extract from Rauwolfia vomitoria. Int J Oncol. 2006 Nov;29(5):1065-73.
- Specific indications include full blooded, red flushed face and ears, prone to anger or anxiety, hypertension.

Albizia julibrissin "Mimosa"

- A semitropical ornamental tree native to Asia.
- In China, it is known as the "**Tree of Happiness**" because of its calming properties; for it is known to 'nourish the heart, calm the spirit and promote joy.'"
- The bark and flowers enhance mental wellness, curb depression, and promote sound sleep.

D. Bensky and X. Gamble, Chinese Herbal Medicine Materia Medica, Eastland Press, Seattle, WA (1993)

Albizia julibrissin Extract (AJE) Modern Research

- Has demonstrated anxiolytic-like effects.
- ABE orally administered at 200 mg/kg to mice. showed an antidepressant-like effect
- Anxiolytic effects of Julibroside in mice
- Enhances all aspects of neurotransmitter secretion and regulation.
- Antidiabetic, renal/hepatic/pancreas/cardiac protective

Prog Neuropsychopharmacol Biol Psychiatry. 2013 Jul 1;44:184-92; *Pharmacol. Biochem. Behav.* **81** (2005), pp. 205–210; *Life Sci.* **75** (2004), pp. 2787–2795. *Pharmacol Biochem Behav.* 2007 May;87(1):41-7; *Altern Med.* 2014 Jul 16;14:243.

***Albizzia julibrissin* (AJ)** **Modern Research in Oncology**



- The “Tree of Happiness” – like rose excellent for sadness and grief.
- Improves immune response by inducing cytokine and chemokines; and by significantly promoting NK cell activity and delaying-type hypersensitivity.
- Triterpenoidal saponins show profound cytotoxic effects.
- Julibroside J(8), one of the triterpenoid saponins, has potent antiangiogenic and anti-cancer effects.

Int Immunopharmacol. 2014 Oct;22(2):346-55; Chem Pharm Bull (Tokyo). 2006 Aug;54(8):1211-2; Bioorg Med Chem Lett. 2005 Oct 15;15(20):4493-5; Phytomedicine. 2009 Aug;16(8):703-11. Epub 2009 May 6.

American Skullcap **(*Scutellaria lateriflora*)**

- Was used by both Native American Indians and the Eclectic physicians to ease anxiety and stress
- Two Eclectic uses:
 - 1) Where there is irritability of the nervous system, with restlessness and nervous excitability; inability to sleep without pain; general irritability with insomnia from local physical causes.
 - 2) where there is nervous disorder, characterized by irregular muscular action, twitching, tremors and restlessness, with or without incoordination.”

ELLINGWOOD, FINLEY M.D. American Materia Medica, Therapeutics and Pharmacognosy – Page 392, 1919.

82

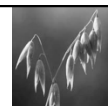
Passion flower **(*Passiflora incarnata*)**



- Antispasmodic, sedative, anxiolytic, GI protective
- Increases ‘glutathione’
- Reduces the inflammatory response by modulation of the liberation or synthesis of histamine and serotonin, by reduction of neutrophil migration, IL-1 β levels, and oxidative stress and nociception.
- **Chrysin**, an active compound found in passiflora) has demonstrated pleiotropic cancer inhibiting mechanisms including inhibiting aromatase, proteasome, VEGF, VEGFR, IL-6,, HIF-1a, NF-kB, COX-2, and through the enhancement of NK cells, and p21 gene expression.

Biochem Pharmacol. 2005 Jun 15;69(12):1815-27; Planta Med. 2006 Jun;72(8):708-14; Mol Cancer Ther. 2007 Jan;6(1):220-6; Neurosci Lett. 2010 Sep 8; AANA J. 2008 Apr;76(2):113-7; J Pharm Pharmacol. 2015 Jul;67(7):1017-27.

Milky Oat Seed () ***Nervine & General Relaxant***



- Strengthens and nourishes the nervous system
- Builds energy, reduces stress and raises the mood
- Helps restore vital energy
- Aids in recovering from illness and/or prolonged times of stress
- Dr. Finley Ellingwood says, “Avena is a remedy of great utility in loss of nerve power and in muscular feebleness from lack of nerve force.”
- Useful in combating various addictions (e.g., tobacco, cannabis, opiates, alcohol etc.)
- Avenanthramides inhibit proliferation of human colon cancer (through inhibition of macrophage PGE(2))

Appl Biochem Biotechnol. 2010 Mar;160(6):1573-84. Epub 2009 Feb 18; Nutr Cancer. 2010;62(8):1007-16.

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Ziziphus (*Ziziphus spinisa*) Seed



- According to TCM classified as sour and balanced, and is mainly used to drain the liver and gallbladder; nourish the blood, and to treat the heart, via "calm the spirit."
- Usually stir-fried prior to use.
- It's central action is for the treatment of Shen deficiency and insomnia.

Zhu Youping, Chinese Materia Medica: Chemistry, Pharmacology, and Applications, 1998
Harwood Academic Publishers, Amsterdam.

Ziziphus Modern Research

- *Ziziphus* and *Magnolia officinalis* bark extracts was tested for tolerability and efficacy in 295 volunteers with mild to moderate sleep difficulties - 86.9%, found it aided restful sleep and 82.8% found it effective in reducing fatigue due to lack of sleep.
- Ziziphus seed extract, caused sedative activity (spontaneous motion assay) and hypnotic activity (sleep) when administered orally to mice.
- Ziziphus and schisandra normalized brain amino acids, and induces relaxation in animals.

Maruyama Y, Kuribara H, Morita M, Yuzurihara M, Weintraub ST: Identification of magnolol and honokiol as anxiolytic agents in extracts of saiboku-to, an oriental herbal medicine. 1998, 61:135-138; Maruyama Y, Kuribara H, Morita M, Yuzurihara M, Weintraub ST: Identification of magnolol and honokiol as anxiolytic agents in extracts of saiboku-to, an oriental herbal medicine. Nat Prod. 1998, 61:135-138; Gao JR, Ji WB, Jiang H, Chen JF: Effects of extracts from ziziphi spinosae semen and schisandrae chinensis fructus on amino acid neurotransmitter in rats with insomnia induced by PCPA. Zhong Yao Cai. 2012 Oct;36(10):1635-9.

Ziziphus jujuba spinisa Cancer research



- **PHY906**, is a decoction of a mixture of the four herbs *Scutellaria baicalensis*, *Glycyrrhiza uralensis*, *Paeonia lactiflora*, and *Ziziphus jujuba* has recently been the center of much cancer.
- **Jujuboside B (1)** is one of the saponins isolated from the seeds of Zizyphus, induced apoptosis and autophagy in AGS and HCT 116 human cancer cells and also effectively suppressed tumor growth in mice (HCT 116 cells).
- The polysaccharides from Ziziphus seed possess antioxidant activity and a hepatoprotective effect, via augmentation of the Nrf2 pathway in liver tissue.

J Ethnopharmacol. 2012 Apr 10;140(3):614-23. Nat Prod. 2014 Feb 28;77(2):370-6; Food Chem Toxicol. 2014 Dec;74:76-84.

PHY906*

* U.S. Patent 7,025,993 B2 ; IND: 62,627

- **Composition**
– Spray dried aqueous extract of four botanicals
- **Traditional use (since 300 A.D.)**
– Diarrhea, vomiting, nausea, intestinal cramping
- **Modern use (2000 A.D.)** : An adjuvant for cancer chemotherapy

Chemotherapeutic Agent	Indication
• CPT-11	• Colorectal Cancer
• Capecitabine, 5-FU	• Liver Cancer
• CPT-11/5-FU/LV	• Colorectal Cancer
• VP-16	• Lung Cancer
• L-OddC	• Leukemia, Pancreatic
• Gemcitabine	• Pancreatic Cancer
• Oxaliplatin	• Colorectal Cancer

PHY906

- Shown to enhance the chemotherapeutic efficacy while decrease chemotherapy-related toxicities and side effects of a variety of anticancer agents in various cancers.
- The PHY906 clinical program consists of five trials in three different types of cancers in both the United States and Taiwan.
- To date, approximately 150 subjects have received PHY906 in combination with chemotherapy in these five clinical studies.

Journal of Ethnopharmacology 140 (2012) 614– 623

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Botanical Extract PHY906 Trial Results

- Did not alter PK/metabolism of 5-FU, Irinotecan or SN-38
- Well tolerated at dose levels of 1.2 gm and 2.4 gm/day with no apparent toxicities
- Reduced severity of diarrhea associated with irinotecan chemotherapy by one grade
- Reduced use of anti-diarrhea medications required to treat irinotecan-mediated diarrhea
- Reduced nausea/vomiting associated with irinotecan
- The combination of PHY906 with irinotecan, 5-FU, and leucovorin (LV) also resulted in **additive antitumor activity with no increased host toxicity.**
- **Significantly improved antitumor activity and overall survival.**

Clin Colorectal Cancer. 2011 Jun;10(2):85-96. doi: 10.1016/j.clcc.2011.03.003. Epub 2011 Apr 22.

Poria Cocos



- Used in Traditional Chinese Medicine (TCM) to improve memory and cognition in old age
- Enhances Vital Spirit - used by Taoist adepts to help attain enlightenment.
- Helps overcome anxiety, worry, and fear
- Immune system tonic (Spleen)

The bark is used mostly to strengthen the Vital Spirit (Spirit Poria), and nervous system, and the inner core, which is more for the Spleen and to drain dampness (fluid retention).

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Poria cocos (continued)

- Used in combination with other herbs
 - Improves learning and memory
 - Inhibits dementia in animals by effecting the M-cholinergic transmitters of the CNS
- A study of 21 depressed patients found that the symptoms of depression had been improved after 6 weeks of treatment of Xiaoyaosan, which consist of *Bupleurum chinense*, *Paeonia lactiflora*, ***Poria cocos***, *Angelica sinensis*, *Zingiber off.*, *Atractylodes macrocephala*, *Glycyrrhiza uralensis*, and *Mentha haplocalyx*.

Phytomedicine 2004; 11(6): 544-548;
Zhongguo Zhong Xi Yi Jie He Za Zhi 1993;
13(11): 675-676, 646.

J Ethnopharmacol. 2014 Oct 15;158PA:
1-10. doi: 10.1016/j.jep.2014.10.005.

Poria's many health-promoting benefits include

- **Anti-inflammatory** *Chemical & Pharmaceutical Bulletin* 1997; 45(3): 492-494, *Journal of Ethnopharmacology* 2000; 73(1-2): 61-69, *Phytochemistry* 1998; 48(8): 1357-1360, *Immunopharmacology and Immunotoxicology* 2004; 26(1): 103-112.
- **Anti-tumor** *Oncology* 1996; 53(5): 382-385, *J Nat Prod.* 2009 Oct;72(10):1786-92, *Carbohydrate Research* 2003; 338(14): 1517-1521; *Breast Cancer Res Treat.* 2010 Jun 3, *Biochemical and Biophysical Research Communications* 2005; 332(4): 1153-1161; *Journal of Natural Products* 2007; 70(6): 948-953, *PLoS One.* 2015; 10(4): e0122270.
- **Topo inhibitor** *Cancer Science* 2004; 95(4): 354-360.
- **Immune system enhancement/ modulation (induce Toll-like receptor 4, down-regulate pro-cancerous chemokines.** *Zhonghua Min Guo Wei Sheng Wu Ji Mian Yi Xue Za Zhi* 1992; 25(1): 1-11.
- **Insulintrophic/anti-diabetic (improves glucose uptake and utilization through GLUT4)** *Eur J Pharmacol.* 2010 Sep 9.
- **Improves learning and memory** *Zhongguo Zhong Xi Yi Jie He Za Zhi* 1993; 13(11): 675-676, 646.
- **Anti-emetic** *Planta Medica* 1995; 61(6): 527-530.

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Saffron (*Crocus sativa*)



- Used for medicinal purposes for millennia to treat various health conditions including: cough, flatulence, stomach disorders, colic, insomnia, chronic uterine hemorrhage, amenorrhea, dysmenorrhea, menstruation, scarlet fever, smallpox, colds, asthma, and cardiovascular disorders.

In TCM it is used as an anodyne, and emmenagogue.
Is a rich source of carotenoids and is a potent cell oxygenator.

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Saffron Antidepressive Effects

- Based on five randomized controlled trials (n = 2 placebo controlled trials, n = 3 antidepressant controlled trials) saffron extract (200-400 mg. daily) improved symptoms of depression in adults with major depressive disorder.
- Crocins are effective in different models of psychiatric disorders including anxiety and depression, and even obsessive compulsive disorders.

J Integr Med. 2013 Nov;11(6):377-83. doi: 10.3736/jintegrmed2013056;
Neurosci Lett. 2012 Oct 18;528(1):27-30

95

Saffron (*Crocus sativa*)

- Crocin, crocetin or safranal, are carotenoids of saffron that have antithrombotic properties, especially anti-Xa activity.
- Antifactor Xa activity is the gold standard for monitoring low molecular weight heparin derivatives.
- Crocetin administration (3 mg/kg), 30 min before the beginning of endotoxin infusion, improved hemostatic indices such as platelet blood counts ($P \leq 0.05$), blood plasma fibrinogen and protein C concentration ($P \leq 0.05$). In addition, it ameliorated fibrin deposition.
- Crocetin possesses a preventive antithrombotic role in vivo

Blood Coagul Fibrinolysis. 2013 Apr;24(3):305-10

96

Saffron anti-cancer effects



- Inhibition of topo II.
- Crocin and dimethyl-crocin exhibit potent cytotoxic effects on human cancer cell lines by disrupting DNA-protein interaction of a cancer cell.
- Shown to inhibit various cancers including colon, bladder, breast, lung and skin.
- Has a protective effects against the chemotherapeutic agent cytosin and cisplatin.
- Potent mood and memory enhancing properties, inhibits chemo-brain, and improves peripheral blood flow.
- Useful for insomnia and anxiety

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American Skullcap Modern research

- In vivo animal behavior trials were performed to test anxiolytic effects in animals orally administered *S. laterifolia* extracts.
- The compounds, baicalin and baicalein, may play a role in the anxiolytic activity and are known to bind to the GABA A receptor (benzodiazepine site) which induces calmness.
- In a recent randomized, double-blind placebo-controlled crossover study on mood in healthy volunteers, American Skullcap extract significantly enhanced global mood without a reduction in energy or cognition.

Phytomedicine. 2003 Nov;10(8):640-9; Phytother Res. 2014 May;28(5):692-8.
doi: 10.1002/ptr.5044. Epub 2013 Jul 22.

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American Skullcap (AS) Cancer inhibiting research

- Significant anti-oxidative and DNA protecting effects of the extract
- **Scutellarein**, a compound within AS, was found to possess anticancer potential against fibrosarcoma (an aggressive form of cancer), in vivo by inhibiting cell migration, invasion and the expression and activity of matrix metalloproteinase (MMP)-2, -9 and -14, and by down regulating NF-kB.
- Also exhibits significant redox-anti-oxidant effects.

Int J Mol Med. 2015 Jan;35(1):31-8; Int J Mol Med. 2015 Jan;35(1):31-8.

99

Lavender (*Lavandula angustifolia*)



- Lavender flower and its extracts have been used, internally, topically, in baths, and by olfaction, for centuries as a treatment for anxiety and depression, as well as for insomnia, and gastrointestinal distress, including "nervous stomach"
- Lifts the Vital Spirit

J Herb Pharmacother. 2004;4(2):63- 78.

100

Healing Baths



- I often recommend healing baths—including Epsom salt, aromatic baths, and herbal diaphoretic therapy—to my patients as part of their protocol.
- 2 cups of Epsom salts with 10-20 drops EO lavender oil
- Light some candles and read sacred/spiritual reading, relax and contemplate.



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Oral lavender oil

- An evidence-based review was recently conducted of an orally administered lavandula oil preparation for anxiety disorder and related conditions was published.
- Seven trials were included, among which four therapeutic trials had a treatment duration of 6 or 10 weeks
- The lavender oil had beneficial effects on typical co-morbidity symptoms of anxiety disorders, for example, disturbed sleep, somatic complaints, or decreased quality of life.

Pract. 2013 Nov;17 Suppl 1:15-22. doi: 10.3109/13651501.2013.813555. Epub 2013 Aug 3.

Lavender oil aromatherapy

- Demonstrated anxiolytic activity in patients in intensive care units
- A study of lavender oil in burner use was conducted on staff mood and stress in a hospital setting.
- A significant number of respondents (85%) believed that the lavender aroma improved the work environment.
- The effects of lavender aromatherapy was studied on depressed mood and anxiety in female patients being treated with chronic hemodialysis
- Lavender aroma significantly decreased anxiety and improved mood and sleep in this group as well.

J Adv Nursing. 1995;21:34-40; Int J Nurs Pract. 2000;6:110-112; J Altern Complement Med. 2005;11(4):631-637

103

Aqueous Extract of *Lavender Angustifolia*

- Inhibits Lymphocytes Proliferation of Hodgkin's Lymphoma Patients
- The effective concentration of Lavender that decreased viability of Hodgkin's lymphoma cells below Lethal Concentration 50 (LC50) value was 100 µg/ml and this was half of the therapeutic dose.
- Apoptosis was the main mechanism the Hodgkin's lymphoma cell encountered when exposed to the aqueous extract of Lavender.

J Cancer Prev. 2013 Fall;6(4):201-8.

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Linalool:

the 'sweetness' of Lavender and other oils

- Has been the subject of numerous studies investigating its anxiolytic (anti-stress) effects. Inhalation of Linalool, extracted from natural essential oil of lavender, leads to decreased aggressive behavior, and an overall reduced stress response.
- Linalool has been shown to inhibit glutamate binding, demonstrating protection against glutamate related toxicity.
- Exhibits cytotoxic effects by activating antitumor immunity.
- Decreases liver cancer cell viability
 - A concentration of 0.4 micromole inhibited 50% of the cells from replicating
- French lavender essential oils often contain between 35% and 50% linalool.

Aromatic Thymes;3(2):11/13; J Cancer Prev. 2013 Fall;6(4):201-8; J Cancer Prev. 2013 Fall;6(4):201-8.

AROMATHERAPY AS AN ADJUVANT TREATMENT IN CANCER CARE

- According to a Cochrane review paper of clinical trials found Aromatherapy improved patient-identified symptom relief, psychological wellbeing and improved sleep.
- The application of aromatherapy is suggested to help patients cope with stress, chronic pain, nausea and depression.
- Neuro-chemical aspects involve a suggested inhibition of glutamate binding, γ -aminobutyric acid (GABA) augmentation and acetylcholine receptor binding.

Boehm et al., Afr J Tradit Complement Altern Med. (2012) 9(4):503-518

106

Rose (*Rosa rugosa*) petals

- Are very relaxing and also remind us of the feelings of love.
- A specific for grief
- A gentle liver tonic (cooling)
- Contains phenolic compounds including, flavonoid, phenolic acid, and tannins, carotenoids, polysaccharides and terpenes (geraniol)
- Cytotoxic, redox-antioxidant, and antimicrobial properties
- Geraniol has cancer chemopreventive efficacy by modulation of multiple molecular pathways including the control of cell cycle and apoptosis

J Sci Food Agric. 2013 Jul 1. doi: 10.1002/jsfa.629; Toxicology (2011), doi:10.1016/j.tox.2011.08.020; Biochemical and Biophysical Research Communications 407 (2011) 129–134

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Geraniol

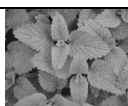
the essential oil of rose and other plants

- Modulates DNA synthesis and potentiates 5-fluorouracil efficacy on human colon tumor xenografts
- Inhibits the growth of human colon cancer.
- Suppresses the growth of A549 human lung cancer cells by inhibiting the mevalonate pathway and RAS in culture and in vivo.
- Significantly increased the antiproliferative and apoptosis-inducing effects of gemcitabine on BXP-3 pancreatic cancer cells.
- Inhibits skin cancer by suppressing COX-2 and the Ras proliferation pathway.

Cancer Letters Volume 215, Issue 1, 8 November 2004, Pages 53-59; J Pharmacol Exp Ther. 2001 Jul;298(1):197-200; Nutr Cancer. 2014;66(5):888-95; J Int Med Res. 2013 Aug;41(4):993-1001; J Appl Toxicol. 2013 Aug;33(8):828-37.

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Melissa officinalis

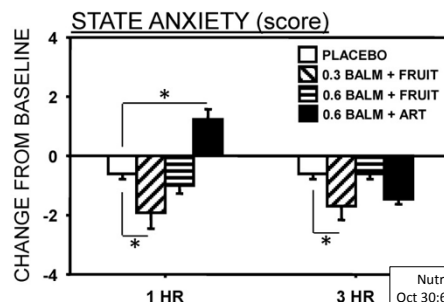


- Has been used historically and contemporarily as a modulator of mood and cognitive function, with anxiolytic effects following administration of capsules, coated tablets and topical application.
- Lemon balm treatments is generally associated with improvements in mood and/or cognitive performance.
- Several studies of a lemon extract performed on animals showed that it is able to reduce the restless state of the animals in a significant way.

Nutrients. 2014 Oct 30;6(11):4805-21. doi: 10.3390/nu6114805; *Psychosom Med.* 2004 Jul-Aug;66(4):607-13; *Neuropsychopharmacology.* 2003;28(10):1871-81. 109

Anti-stress effects of lemon balm-containing

There was a significant reduction in state anxiety following the 0.3 g lemon balm/fruit drink at both 1 and 3 h post drink



Melissa officinalis and Passiflora infusion as physiological stress deceiver

- A study was conducted to determine the effect of a Lemon balm and Passion flower infusion on the severity of physiological chronic stress induced by movement restriction in mice.
- The mice given the herbal infusion had lower plasma corticosterone levels, which is the most important biomarker associated with physiological stress, demonstrating a anti-stress effect.
- A combination of Lemon balm and valerian (600 mg. total) possesses profound anxiolytic properties.

Int J Clin Exp Med. 2013 Jun 26;6(6):444-51; *Phytother Res.* 2006 Feb;20(2):96-102. 111

Melissa off. essential oil: antitumoral and antioxidant activities



- Has been used historically and contemporarily as a modulator of mood and cognitive function, with anxiolytic effects following administration of capsules, coated tablets and topical application.
- An in-vitro cytotoxicity assay indicated that this oil was very effective against a series of human cancer cell lines (A549, MCF-7, Caco-2, HL-60, K562) and a mouse cell line (B16F10).
- Topically has demonstrated significant protection against herpes outbreaks (especially stress-related)

J Pharm Pharmacol. 2004 May;56(5):677-81; *Nat Prod Res.* 2008;22(16):1433-40. 112

Ashwagandha (*Withania Somnifera*)



- Primary Adaptogen – induces “restful sleep” and makes us “strong as a horse.”
- Inhibits age-related chronic diseases including cancer, senile dementia and AD.
- Enhances work production, energy, learning and memory.
- Anxiolytic (GABA-like activity) and antidepressant.
- Active compounds: steroidal lactones (withanolides, withaferins)

Yance, D. Adaptogens in Medical Herbalism, Healing Arts Press, 2013, Ashwagandha monograph, pg. 361-368

113

Ashwagandha extract (AE) for anxiety: a systematic review of human trial results

- Sixty-two abstracts were screened; Five human trials met inclusion criteria.
- All five human studies concluded that AE intervention resulted in greater score improvements (significantly in most cases) than placebo in outcomes on anxiety or stress scales.

Pratte MA, Nanavati KB, Young V, Morley CP. An alternative treatment for **anxiety**: a systematic review of human trial results reported for the Ayurvedic herb **ashwagandha** (*Withania somnifera*). J Altern Complement Med. 2014 Dec;20(12):901-8.

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Ashwagandha in Oncology

- Significantly increased the stress-induced depleted T-cells and increased the expression of Th1 cytokines
- Antioxidant protection - enhances superoxide dismutase, catalase and glutathione
- Inhibition of NK-Kb and AP-1
- Significant increase in WBCs and platelets in animals treated
- Protective effect against myelo-suppression - Cytotoxin-induced immune-suppression was counteracted
- Taken with taxol caused significant reversal of neutropenia and overall protective effects against taxol-induced toxicity

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Withaferin A (WA) targets heat shock protein 90

- WA, a steroidal lactone occurring in *Withania somnifera*, in pancreatic cancer in vitro and in vivo.
- WA exhibited potent antiproliferative activity against pancreatic cancer cells in vitro in pancreatic cancer cell lines Panc-1, MiaPaCa2 and BxPc3, respectively
- WA binds Hsp90, inhibits Hsp90 chaperone activity through an ATP-independent mechanism, results in Hsp90 client protein degradation, and exhibits in vivo anticancer activity against pancreatic cancer.
- WA strongly inhibited the survival of several human and murine B cell lymphoma cell lines.
- WA strongly inhibited the survival of several human and murine B cell lymphoma cell lines.

Biochem Pharmacol. 2010 Feb 15;79(4):542-51. doi: 10.1016/j.bcp.2009.09.017; **Cancer Biol Ther.** 2015 May 28:0.

Ocimum sanctum (Holy basil) 'Tulsi'



Has been used for thousands of years in Ayurveda for its diverse healing properties.

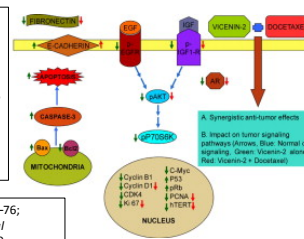
- **"Tulsi"** means **"The Incomparable One,"** a sacred herb, used traditionally for thousands of years in ceremonial worship and as a medicine - "rasayana" means "path of Essence"
- Most traditional homes and temples in India will have at least one tulsi plant.
- Builds Vital Force & Spirit
- Active compounds: eugenol, ursolic acid (anti-tumor compound), rosmarinic acid, **vicenin-2** etc.

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Ocimum sanctum (Holy basil) 'Tulsi' **The Incomparable One,"**

Anti-cancer effects of Holy basil derived flavonoid vicenin-2 as a single agent and in synergistic combination with docetaxel in prostate cancer

Lowers the stress-induced release of adrenal hormones and assists in the normalization of cortisol



Phytomedicine 1(1) (1994): 63–76;
"Indian Journal of Experimental
Biology 40(10) (2002): 1151–60

Biochemical Pharmacology, Volume 82, Issue 6, 2011, 1100–1108

118

Shatavari: Modern research

- Nourishes Inward Kidney Essence – soothes, moistens
- Immune-modulatory – Balances Th1/Th2 immunity
- Reduced the tumor incidence in animals treated with tumor inducing DMBA.
- Shatavarins are **steroidal saponins** that possess direct anticancer activity in vitro and in vivo.
- The shatavarins (specifically shataverin IV) exhibits significant anticancer activity in vivo against Ehrlich ascites carcinoma.
- Oral administration to tumor bearing mice at doses of 250 and 500 mg/kg body weight for 10 days, showed significant reduction in percent increase in body weight, tumor volume, packed cell volume, viable tumor cell count, and increased non-viable cell count when compared to the untreated mice.

J Ethnopharmacol. 2009 Jan 21;121(2):241-7. Epub 2008 Nov 8; Int J Cancer 1981; 28:607-10; Indian J Pharmacol. 2012 Nov-Dec; 44(6): 732–736.

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Gotu kola (*Centella asiatica*)



Constituents: triterpenoids (asiaticoside, madecassoside, madasiatic acid, terpene acetate, camphor, cineol, glycerides, fatty acids, various plant sterols and polyacetylene compounds.

Actions

- Wound Healing (topically applied)
- Connective tissue - anti-Scarring agent (topically applied)
- Circulation improvements
- Memory improvements
- Neuroprotective - revitalizes the nerves and brain cells.
- Anti-stress
- Varicose veins, vein tone
- Chronic hepatic disorders/anti-fibrotic
- Redox/anti-Ox - Cancer preventive
- Modulates angiogenesis

Pharmacol Biochem Behav. 2014 Mar 11; Int J Mol Med. 2012 Dec;30(6):1349-56; Phytother Res. 2009 Jan;23(1):14-9; PLoS One. 2011;6(8):e22745. Epub 2011 Aug 3.

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Asiatic acid (AA) is a pentacyclic triterpenoid within *Centella a.*



- Increases brain levels of GABA, relaxing the nervous system.
- Profound neuroprotective effect – enhancement of GSH, thiols and redox-antioxidant machinery in the brain
- Has been shown to reduce inflammation, inhibit tumor cell proliferation, and induce apoptosis through a mitochondria-dependent pathway.
- Inhibits transcription factor NF- κ B, p38 MAP and ERK kinases in a variety of tumor cells.
- Demonstrates anti-angiogenic and anti-metastatic potential in vivo animal studies.
- Protective healthy cells from the toxic effects of chemotherapy - Antigenotoxic

NeuroToxicology 29 (2008) 948–957; The Journal of Toxicological Sciences Vol. 35 (2010) , No. 1 February 41-47; Cancer Letters 320 (2012) 158–170; Babykutty et al. *Mol. Cell. Toxicol.* 30 (2009) 5–13; D. 16 *Toxicol. In Vitro*

Hops (*Humulus lupulus*)

- Traditional usage: Insomnia, Nervous anxiety, irritability, and as Anti-aphrodisiac
- Used quite widely by the Eclectic physicians in a specific medicine known as "Lupulin."
- Sedative, hypnotic, and astringent properties, as well as mild estrogenic constituents.
- As a bitter it was also used for the treatment of gastritis, colitis, and indigestion.
- Active compounds: prenylflavonoids, including prenylnaringenin, xanthohumol, and isoxanthohumol

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Hops extract research

- A unique standardized extract (Lifenol from hops, rich in prenylflavonoids including 8-PN has been clinically proven to relieve menopausal symptoms.
- 8-PN is effective agent for the prevention and treatment of osteoporosis.
- Xanthohumol is a potent anti-inflammatory: Inhibits TNF- α and Monocyte Chemoattractant Protein-1.
- Xanthohumol is a very potent cancer chemopreventive agent through diverse mechanisms which include inhibition of platelet activation.

J Agric Food Chem. 2005 Aug 10;53(16):6281-8. Br J Nutr. 2007 Nov;98(5):950-9. Epub 2007 May 23. J Endocrinol. 2006 Nov;191(2):399-405; Planta Med. 2008 Jun;74(8):794-801. Epub 2008 Jun 6; Phytother Res. 2009 Jun;23(6):851-8; Xanthohumol.

Hops extract research

- Hops extract (in higher doses) improves sleep and is effective for insomnia
- Also, prolonged use in high dose is effective as an anti-aphrodisiac.
- Anti-mutagenic Hop flavonoids have anti-breast cancer effects in part through aromatase inhibition.
- Prenylflavonoids inhibitor the efflux transporter breast cancer resistance protein (BCRP/ABCG2).
- Linalool as a component of Hops promotes doxorubicin-induced antitumor activity

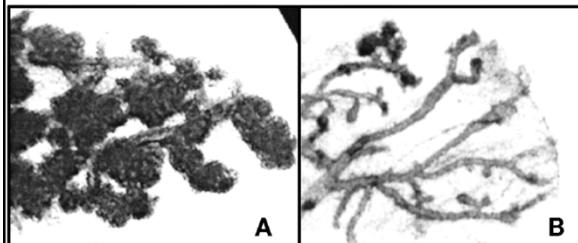
Holist Nurs Pract. 2009 Jul-Aug;23(4):253-6. Wien Med Wochenschr. 2007;157(13-14):367-70. Review; J Ethnopharmacol. 2009 Aug 17;125(1):36-40. Epub 2009 Jun 26; Phytomedicine. 2008 Mar;15(3):216-20. Epub 2007 Oct 23; J Steroid Biochem Mol Biol. 2007 Jun-Jul;105(1-5):124-30. Epub 2007 Jul 23; Food Chem Toxicol. 2013 Mar;53:174-9

Hops extract anti-prostate cancer effects

- Hops extract and specific compounds in hops including xanthohumol, suppress prostate cancer.
- Xanthohumol prevents the AR receptor from translocating to the cell nucleus, thus inhibiting its potential to stimulate the secretion of PSA and other hormone-dependent effects
- Xanthohumol suppresses Prostate cancer in part by inhibiting NF- κ B
- Treatment of PC-3 and DU145 prostate cancer cells by prenylflavonoids induces a caspase-independent form of cell death.

Amer Ass for Cancer Research Frontiers in Cancer, Prevention Research Conference, held in Houston, Dec. 6-9, 2009; Cancer Letters, Volume 246, Issues 1-2, 8 February 2007, Pages 201-209; Phytother Res. 2008 Feb;22(2):197-203, Phytomedicine. 2006 Nov;13(9-10):732-4. Epub 2006 May 5

Hops extract suppresses Breast cancer growth in mouse mammary glands



Gerhauser C et al. Mol Cancer Ther 2002;1:959-969

©2002 by American Association for Cancer Research

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Blue Vervain *Verbena officinalis*



- Has been used in traditional herbal medicine by many diverse cultures from the ancient Romans and Celtic cultures to the American Indians.
- Has been considered a heal-all, being used to treat ailments of several body systems.
- Assist digestion having an overall calming effect, bitter compounds enhance liver health.
- It is well-known for its relaxing effect on the nervous system.
- Has novel neuroprotective effects, exerts cytoprotective effects on cells of the central nervous system.
- Significantly attenuated the toxicity of β -amyloid (A β) peptide and reducing the accumulation of A β peptide is an important cytotoxic factor involved in Alzheimer's disease.

Owen N. Verbena officinalis L., British Journal of Phytotherapy, (2001;5, No. 3:114-117), Neuropharmacology Volume 50, Issue 6, May 2006, Pages 641-650

In-vivo anti-tumor activity of *Verbena officinalis* extract (VOE)



- Has been used in traditional herbal medicine by many diverse cultures from the ancient Romans and Celtic cultures to the American Indians.
- Well-known for its relaxing effect on the nervous system.
- The active compounds are iridoid glycosides such as verbenalin and its derivatives; and flavonoid compounds such as luteolin, kaempferol and ursolic acid
- The anti-tumor effects of VOE on H22 (Liver cancer) tumor-bearing mice and its effect on immune function.
- VOE had anti-tumor effect, with the inhibition rate reaching 38.78%, it also increased the spleen index demonstrating immune enhancing activity as well.

Afr J Tradit Complement Altern Med. 2013 Apr 12;10(3):512-7. eCollection 2013.

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Pulsatilla vulgaris/chinensis/koreana (Pasque-flower)



- **Traditional usage and specific indications (drop dosing of the fresh extract):**
 - Melancholic, nervousness with despondency, sadness and disposition to weep.
 - For worry and fear in the pale (anemic) shy types; in women passing through menopause. For morbid mental excitation associated with physical debility; marked depression of spirits; insomnia, with nervous exhaustion; pain, with debility.
 - A remedy for nervous headaches, especially if of the anemic variety.

Ellingwood, F., Amer. Materia Medica Therapeutics and Pharmacognosy, Cincinnati, OH, 1919, Pg. 149-152 129

Pulsatilla saponins



- *Pulsatilla chinensis* (Bai tou weng in Mandarin), is prescribed to clear heat and detoxify fire poison.
- It is used in damp heat conditions of the stomach and large intestine in dysentery.
- **Pulsatilla saponin A**, an active molecule from *Pulsatilla chinensis*, induces cancer cell death and inhibits tumor growth in mouse xenograft models.
- **Pulsatilla saponin D**, from *Pulsatilla koreana*, targets c-Met and exerts potent antiangiogenic and antitumor activities in gastric cancer.
- Akt and mTOR were also inhibited.

J Surg Res. 2014 May 15;188(2):387-95. doi: 10.1016/j.jss.2014.01.026. Epub 2014 Jan 24; Carcinogenesis. 2013 Sep;34(9):2156-69. doi: 10.1093/carcin/bgt159. Epub 2013 May

Valerian (*Valeriana officinalis*)

- From the Latin word *valere*, which means *to be in good health*.
- The herb was first discovered and used by Greek physicians, who recommended it for a host of medicinal uses:
 - Insomnia – with deficient blood (cerebral anemia)
 - Anxiety
 - Spasm



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Valepotriates potential anti-tumor compounds

- Both *V. off.* and *jatamansi* fresh root extracts exhibit cytotoxicity against a wide variety of cancer cells.
- IVHD-valtrate from *V. jatamansi*, inhibited the growth and proliferation of ovarian cancer cell lines in a concentration-dependent manner, and in vivo arrested the ovarian cancer cells in the G2/M phase and induced apoptosis, and significantly suppressed the growth of A2780 and OVCAR3 xenograft tumors.
- Increase sp53, Rb, p21, p27, down-regulates Bcl-2/Bax and Bcl-2/Bad ratio and enhances the cleavage of PARP and Caspases
- Minor valepotriates from *V. jatamansi* are cytotoxicity against metastatic prostate cancer cells

Planta Med. 1983 Nov;49(3):138-42; Phytomedicine. 1998 May;5(3):219-25; Planta Med. 2014 Dec 3; Curr Cancer Drug Targets. 2013 May;13(4):472-83; Planta Med. 2015 Jan;81(1):56-61.

Ginger (*Zingiber Officinale*)



Bioorg Med Chem. 2010 May 1;
18(9):3345-51.

- Therapeutic effects: Arthritis, heart tissue, motion sickness, nausea and cancer and heart disease.
- Animal studies suggest ginger reduces anxiety.
- Ginger extract identified nine compounds that interact with the human serotonin 5-HT_{1A} receptor with significant to moderate binding affinities

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Andrographis paniculata (AP) extract and pure Andrographolide inhibit chronic stress-triggered cancers in animals

- Mediates stress-related inflammation by suppressing the blood IL-1 β and IL-10 as well as brain TNF- α and IL-10 expressions induced by chronic stress
- Both AP and andrographolide are pharmacologically polyvalent anti-stress agents, and that biological processes regulating corticosterone and cytokine homeostasis are involved in their modes of actions.

Cell Mol Neurobiol. 2014 Nov;34(8):1111-21. doi: 10.1007/s10571-014-0086-1.

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L-Theanine

An amino acid derivative found in tea (*Camellia* sp)

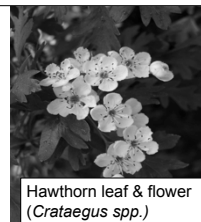
- Works to diminish stress, worry, and anxiety, allowing the brain to focus and concentrate better.
- Studies have shown that the ability to learn and remember may be enhanced with theanine supplementation.
- It not only reduces anxiety but also attenuates the blood-pressure increase in high-stress-response adults.
- Enhances the cytotoxicity of chemotherapy, inhibits MDR, and protects healthy cells of the toxicity of chemotherapy.

AANA J. 2009 Dec;77(6):445-9; J Physiol Anthropol. 2012 Oct 29;31:28

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Closing Quotes

Our task must be to free ourselves by widening our circle of compassion to embrace all humanity and the whole of nature in its beauty." – Albert Einstein



Hawthorn leaf & flower
(*Crataegus* spp.)

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The word "health" originates (old English word Hal) in the words "heal," "whole," and "body," (in Latin, 'Mederi' means to heal and make whole).

True health is wholeness of spirit, mind, and body, and involves the spirit and the breath of God.

We see God both "through" and "in" Nature, which moves in God's order, where there are few straight lines or perfect squares.

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In the words of Eli Jones:

"When I can help a doctor cure a patient I feel just as happy as if it was my own patient. We are here in this world to help each other, and it is one of the things that sweetens our life when we can hold out a helping hand to a brother, or sister, physician. No man liveth to himself."

- Dr. Eli Jones (1908)

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"Cancer is not a curse nor is it a gift; it all depends on how we choose to respond to it."



"Start by doing what is necessary, then what is possible, and suddenly you are doing the impossible."

St. Francis of Assisi