Of Herbs and Vitamins

Tomato Juice for Diabetics

Several life saving medications have their origins in herbs. Classic examples include quinine and artimisine for falciparum malaria, vincristine for hematological malignancies, digitalis for congestive heart failure and salicylates for rheumatic disorders. Humanity has benefited much from scientific investigations on herbs. Lazarus et al.1, in their research letter to JAMA, report an aspirin-like anti-platelet effect of tomato juice in diabetics which may decrease cardiovascular complications in such individuals. They investigated 20 type 2 diabetic patients older than 40 years with HbA1c levels demonstrating a range of poor to good glycemic control. In a double blind study design, after 3 weeks of therapy with 250mL of tomato juice daily, they found that the platelet aggregation in the treated group compared to the control group given tomato-flavoured beverage, was significantly reduced, while HbA1c levels remained unchanged.

1. Lazarus SA et al. Tomato juice and platelet aggregation in type 2 diabetes. JAMA 2004;292:805-6.

Turmeric (haldi) derivative, a cure for cystic fibrosis

Cystic fibrosis (CF) is a genetic disorder affecting 1 in 2000 children of Caucasian origin. The disease results from mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene, transmitted in a recessive fashion. The most common mutation is DF508 which results in the production of a functional but misfolded CFTR protein. This is retained in the endoplasmic reticulum (ER) and targeted for degradation. The retention of misfolded proteins in ER is done through chaperone proteins many of which are calcium dependent. Thus calcium reducing agents can potentially liberate the mutated protein from ER and allow it to reach the plasma membrane and function as the chloride channel, alleviating the disorder. ER calcium pump inhibitors have been shown to have this effect but possess high toxicity. Curcumin, a Turmeric derivative, has been shown to be a low affinity inhibitor of ER calcium pump and is tolerated well in extremely large doses by humans. Thus, Egan et al.1 tested whether oral treatment with curcumin of CFTR DF508 transgenic mice would result in alleviation of CF. Mice were fed 45mg / kg body weight of curcumin for 3 days. Treated mice had dramatically increased survival rates and normal chloride transport across nasal and rectal epithelia. The sodium potential across the epithelia was reduced suggesting sufficient DF508 protein reached the plasma membrane. In vitro experiments confirmed that curcumin treatment resulted in functional plasma membrane localization of the mutated CFTR protein. Human clinical trials for curcumin are anxiously awaited, which would bring this herbal therapy to the forefront of clinical medicine.

1. Egan ME et al. Curcumin, a major constituent of turmeric, corrects cystic fibrosis defects. Science. 2004;304::600-2.

Guidelines for ST-elevation MI / CABG

Reports for 2004, of the American College of Cardiology and American Heart Association on ST-elevation myocardial infarction1 and coronary artery bypass graft surgery2 have been published in Circulation.

Circulation. 2004; 110:588-636.

2. Circulation. 2004; 110:1168-117

Vitamin E and Cardiovascular Disease

The American Heart Association Science Advisory Committee reviewed the recent randomized clinical trials (RCT) for vitamin E and the risk for cardiovascular disease (CVD).1 They conclude that the RCTs vary in terms of the dosage, form and milieu of vitamin E as well as study end-points, duration and populations. Overall the findings are in general agreement with a meta-analysis, previously published2, that scientific evidence does not favour routine use of vitamin E/antioxidant supplements for the prevention and treatment of CVD. Indeed this finding is in contrast to the positive findings of the basic science literature.

1. Kris-Etherton PM. Nutrition Committee of the American Heart Association Council on Nutrition, Physical Activity, and Metabolism. Antioxidant vitamin supplements and cardiovascular disease. Circulation 2004;110:637-41.
2. Vivekananthan DP. Use of antioxidant vitamins for the prevention of cardiovascular disease: meta-analysis of randomised trials. Lancet. 2003 Jun 14;361(9374):2017-23. Erratum in: Lancet. 2004;363:662.

Vitamin E for Common Cold

Vitamin E or alpha-tocopherol blasted its way into the clinic when a RCT demonstrated that daily intake of 2000 I.U of the vitamin slows the progression of Alzheimer's.1 Thus vitamin E is now standard therapy for alzheimer's, however, its role is conflicting in other diseases. Respiratory tract infections (RTI) are prevalent in the elderly and are a cause of high mortality. Meydani et al.2 explored the role of vitamin E in RTI in the elderly. Patients were supplemented with low dose vitamin E (200 I.U). The study found that vitamin E had a protective effect on the frequency of common cold (P=0.04) but it did not affect the frequency or severity of lower RTI.

1. Sano M. A controlled trial of selegiline, alpha-tocopherol, or both as treatment for Alzheimer's disease. The Alzheimer's Disease Cooperative Study. N Engl J Med. 1997;336:1216-22.
2. Meydani SN. Vitamin E and respiratory tract infections in elderly nursing home residents: a randomized controlled trial. JAMA 2004;292:828-36.

Vitamin E and Cancer

Ashfaq et al.1 conducted an elegant experiment on the natural killer (NK) cell tumorilytic activity after treatment with vitamin E in vitro and in a mouse model. They found that NK cell anti-tumor activity was significantly increased after both in vitro and in vivo treatment with vitamin E. Palm oil contains high concentrations of vitamin E and was shown to have similar effect. At a recent conference of the New York Academy of Sciences, Dr. Kalanithi Nesaretnam of the Malaysian Palm Oil Board, Kuala Lampur (KL) presented her findings that g-form of vitamin E inhibits breast cancer cell growth in a mouse model.2 Her group has begun a clinical trial in KL to investigate the effects of vitamin E in combination with tamoxifen in women with stage 1 and 2 estrogen-dependent breast cancer3, as special forms of vitamin E have been shown to have antiproliferative effects in combination with tamoxifen in vitro. Using microarray technology the group has also shown that vitamin E anti-cancer activity is a result of its ability to alter gene expression in breast cancer cell lines and is not limited to the anti-oxidant effect of the vitamin. Stone et al.4 investigated the role of the g-form of vitamin E in colon cancer and discovered that this form down regulates the expression of an oncogene ras-p21 and upregulates the PPAR-g gene, which is involved in inducing apoptosis. The anti-diabetic drug, troglitazone is able to activate PPAR-g and g-tocopherol has structural similarities with troglitazone, making it a potentially strong, relatively non-toxic, anti-cancer drug.

1. Ashfaq MK. Vitamin E and beta-carotene affect natural killer cell function. Int J Food Sci Nutr 2000;51:S13-20.
2. Nesaretnam K. Effect of palm oil carotene on breast cancer tumorigenicity in nude mice. Lipids. 2002;37:557-60.
3. Friedrich MJ. To "E" or not to "E," vitamin E's role in health and disease is the question. JAMA. 2004;292:671-3.
4. Stone WL. The influence of dietary iron and tocopherols on oxidative stress and ras-p21 levels in the colon. Cancer Detect Prev 2002;26:78-84.

Childhood Vaccinations

Chicken pox (varicella zoster) is a highly contagious disease. In the US alone 4 million cases occur annually and 100 deaths result. A population based household contact study was carried out by Seward and colleagues to investigate the effectiveness of the varicella vaccine under the most intense conditions of exposure.1 The vaccine was found to be highly effective for preventing moderate to severe disease. Thus secondary infection in vaccinated individuals was less intense. Also vaccinated children were about 5 times less likely to contract the infection when exposed. Vaccinated children with chicken pox were half as contagious as unvaccinated cases though this was dependent on the severity of infection which was reduced by the vaccine in the first place. Thus varicella vaccine is recommended in household contacts of cases to prevent severe disease and in all children to reduce secondary attack rates, severity and contagiousness.

Another population based study, also published in JAMA, reported on the risk of developing febrile seizures following measles, mumps and rubella (MMR) vaccination2 Out of the about five hundred thousand children vaccinated with MMR, 4%

developed febrile seizures of which 5% occurred within 2 weeks of the vaccination. This study investigated the confounding factors for febrile seizures such as family history, perinatal factors .etc and found that MMR vaccination was associated with a transient increased rate of febrile seizures but the risk was small even in high risk children. The long-term risk of epilepsy was the same as for febrile seizures of any other etiology.

1. Seward JF et al. Contagiousness of varicella in vaccinated cases: a household contact study. JAMA. 2004 Aug 11;292:704-8.
2. Vestergaard M et al. MMR vaccination and febrile seizures: evaluation of susceptible subgroups and long-term prognosis. JAMA 2004;292:351-7.

Changing face of Muscle Physiology

Intense muscle activity leads to muscle fatigue, a phenomenon characterized by reduced force and velocity of contraction. During exercise anaerobic respiration in myocytes results in lactic acid production which is thought to contribute to muscle fatigue by lowering pH which decreases the sensitivity of the contractile apparatus to calcium.1 However, another factor in muscle fatigue is the reduced ability of the sarcoplasmic T-system to conduct action potentials (AP) due to accumulation of potassium, leading to membrane depolarization. Pedersen and colleagues2 used an ingenious technique of skinning the surface membrane of the muscle to allow them direct access to the intracellular environment. They found that acidosis increases the contractile force. They also observed that acidosis reduces the chloride permeability across the membrane. Thus they propose that during muscle fatigue extracellular potassium accumulates causing a reduction in AP generation. Acidosis induced by lactic acid, acts to reduce chloride permeability across the membrane, preventing the membrane potential from decreasing further, thereby reducing the size of the sodium current needed to generate a propagating AP. Thus, down-regulation of chloride permeability by intracellular acidosis is important in preserving a fully functional T system in working muscle.

1. Allen D, Westerblad H. Physiology. Lactic acid--the latest performance-enhancing drug. Science. 2004;305:1112-3.
2. Pedersen TH et al. Intracellular acidosis enhances the excitability of working muscle. Science. 2004;305:1144-7.