**Oxidative stress causes human diseases**

**Role of lycopene, alpha-tocopherol, vit. A, vit. C, zinc, and selenium as anti-oxidant defenses**

**OXIDATIVE STRESS IN THE PATHOPHYSIOLOGY OF HUMAN DISORDERS AND DISEASES**

Oxidative stress is mainly caused by an imbalance between the activity of endogenous pro-oxidative enzymes (such as NADPH oxidase, xanthine oxidase or the mitochondrial respiratory chain) and antioxidant enzymes (such as superoxide dismutase, glutathione peroxidase, heme oxygenase, thioredoxin peroxidase/peroxiredoxin, catalase and paraoxonase).

Endogenous reactive intermediates including photoexcited states of tissue chromophores, reactive oxygen species (ROS), reactive carbonyl species (RCS), transition metal ions, and Schiff bases have been implicated in the initiation and progression of diverse human pathologies including tumorigenesis, atherosclerosis, diabetes, and neurodegenerative disease. Oxidative stress is also implicated in the cognitive deterioration associated with normal aging as well as neurodegenerative disorders such as Alzheimer’s and Parkinson’s diseases.

**OXIDATIVE STRESS IN VASCULAR DISEASE**

Endothelial cells control vascular homeostasis by generating paracrine factors that regulate vascular tone, inhibit platelet function, prevent adhesion of leukocytes, and limit proliferation of vascular smooth muscle. The dominant factor responsible for many of those effects is endothelium-derived nitric oxide (NO).

Endothelial dysfunction characterized by enhanced inactivation or reduced synthesis of NO, alone or in combination, is seen in conjunction with risk factors for cardiovascular disease. Endothelial dysfunction can promote vasospasm, thrombosis, vascular inflammation, and proliferation of the intima.

Vascular oxidative stress and increased production of reactive oxygen species contributes to mechanisms of vascular dysfunction and has been implicated to play an important role in a number of cardiovascular pathologies, including hypertension, atherosclerosis, myocardial infarction, ischemia/reperfusion injury, and restenosis after angioplasty or venous bypass grafting.

The formation of reactive oxygen species is balanced out by antioxidant defenses, and augmenting this defense by antioxidant therapies could therefore provide a potential means to treat conditions in which the formation of reactive oxygen species exceeds the capability of natural protective mechanisms.

**IMMUNOMODULATORY EFFECTS OF LYCOPENE**

There is evidence indicating that regular consumption of tomato products is associated with favorable immunomodulatory effects. In addition, tomato extracts have been shown to possess antioxidant, anticarcinogenic and antithrombotic activity in vitro. The present work was designed to examine the in vitro effect of lycopene on cytokine production by peripheral blood mononuclear cells (PBMC) from 15 healthy subjects. Lycopene is considered to be a potent antioxidant with benefits in prevention of several chronic diseases.

Lycopene induced a dose-dependent increase in IL–1beta, and TNF–alpha production and a decrease in IL–2, IL–10 and IFN–gamma secretion, whereas IL–6 and IL–1ra was not affected.
It was concluded that understanding the role of lycopene in modulation of the immune system may promote decisions as for dietary supplementation of lycopene for reducing the risk of certain diseases.3

LYCOPENE IN THE PREVENTION OF PROSTATE CANCER
Based on the evidence from epidemiologic, animal, and in vitro data and human clinical trials, it is evident that lycopene, a non–provitamin A carotenoid, is a promising agent for prostate cancer chemoprevention. Based on reviews, there is enough evidence to warrant use of lycopene in phase I and II clinical trials to examine its safety and efficacy as a potential chemopreventive agent for prostate cancer.6

VITAMIN E
Vitamin E is a generic term that refers to a family of compounds that is further divided into two subgroups called tocopherols and tocotrienols. It comprises eight different isoforms: four tocopherols (alpha, beta, gamma, and delta) and four tocotrienols (alpha, beta, gamma, and delta). A wealth of data is available for the preventive efficacy of alpha–tocopherol. It is an established antioxidant with an ability to ameliorate the UV–induced skin damage and chemically–induced inflammation in lungs. alpha–T supplementation in human subjects and animal models has been shown to be antioxidant and antiinflammatory in terms of decreasing C–reactive protein (CRP) and release of proinflammatory cytokines, the chemokine IL–8 and PAI–1 levels, especially at high doses.5

In patients with moderately severe impairment from Alzheimer’s disease, treatment with alpha–T slows the progression of disease. Vitamin E may reduce the risk of developing physically debilitating disorders, and Vitamin E antioxidants can help support a strong immune system. Experts also concluded that in patients with angiographically proven symptomatic coronary atherosclerosis, alpha–tocopherol treatment substantially reduces the rate of non–fatal MI, with beneficial effects apparent after 1 year of treatment.6

EFFECT OF ALPHA–TOCOPHEROL ON ANTIOXIDANT ENZYME STATUS
The relationships between alpha–tocopherol, pro–oxidant and antioxidant enzyme status, and radiation toxicity were studied in stage II, III, and IVA oral squamous cell carcinoma patients. It was seen that alpha–tocopherol played a role in protecting against the damage caused by irradiation in oral squamous cell carcinoma patients treated with radiotherapy, by enhancing the antioxidant enzyme status and reducing the pro–oxidant status.7

VITAMIN A
Vitamin A (retinol), an essential human nutrient, plays an important role in cellular differentiation, regulation of epidermal cell growth and normal cell maintenance. Vitamin A also plays an important role in bone structure and function. Notably during pregnancy and throughout the breastfeeding period, vitamin A has an important role in the healthy development of the fetus and the newborn, with lung development and maturation being particularly important.8 The carotenoids, specifically beta–carotene has shown to possess antioxidant properties. This precursor of vitamin A is considered the most efficient “quencher” of singlet oxygen.

THE ROLE OF SELENIUM
Selenium functions as a part of proteins known as selenoproteins. Despite the low selenium content in the body (20–40 mg), selenoenzymes play an important role in antioxidant defense in humans. Through these selenoproteins, selenium functions as a defensive mechanism for oxidative stress, for the regulation of thyroid hormone activity, and for the redox status of vitamin C and other molecules.

In several of its roles, selenium functions as a dietary antioxidant and thus has been studied for its possible role in chronic diseases.9,10 Studies have demonstrated that selenium supplementation reduces the incidence of cancer, particularly prostate cancer.11

EFFECT OF VITAMIN E AND SELENIUM IN PULMONARY TB PATIENTS
Increased production of reactive oxygen species secondary to phagocyte respiratory burst occurs in pulmonary tuberculosis (TB). The present study evaluated the efficacy of vitamin E–selenium on oxidative stress in newly diagnosed patients treated for pulmonary TB. The intervention group (n = 17) received vitamin E and selenium (vitamin E: 140 mg alpha–tocopherol and selenium: 200 microg) and the control group (n = 18) received placebo. Both groups received standard anti–TB treatment. It was concluded that a 2–month intervention with vitamin E and selenium supplementation reduces oxidative stress and enhances total antioxidant status in patients with pulmonary TB treated with standard chemotherapy.12

VITAMIN C IN CHRONIC DISEASE AND EFFECT ON CLINICAL CONDITIONS
Vitamin C is an essential dietary nutrient required as a co–factor for many enzymes. The reduced form of the vitamin, ascorbic acid, is an especially effective antioxidant owing to its high electron–donating power and ready conversion back to the active reduced form. The evidence that ascorbic acid acts as an important antioxidant in many body tissues is convincing.

There is great interest in the clinical roles of vitamin C because of evidence that oxidative damage is a root cause of, or at least associated with, many diseases. A large number of randomized controlled intervention trials document that adequate intakes of vitamin C ameliorate symptoms and shorten the duration of respiratory tract infections, including common cold. Furthermore, vitamin C reduces the incidence and improves outcome of pneumonia, malaria, and diarrhea infections, especially in children in developing countries. The new higher Recommended Dietary Allowance (RDA) for vitamin C of 75 mg for women and 90 mg for men is, for the first time, based on the vitamin’s role as an antioxidant as well as protection from deficiency.13,14

<table>
<thead>
<tr>
<th>Drug</th>
<th>Composition</th>
<th>Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>LYCOPHEROL</td>
<td>Alphatocopherol Acetate IP 10 mg, Vitamin A Acetate IP 2500 IU, Zinc Sulphate Monohydrate U.S.P. eq to Elemental Zinc 27.45 mg, Lycopene USP 2 mg, Selenium Dioxide Monohydrate USP 70 mcg, Vitamin C (coated) IP  25 mg</td>
<td>1 OD</td>
</tr>
</tbody>
</table>
**EFFECTS OF VITAMIN E, VITAMIN C, AND SELENIUM**

Cadmium is a highly toxic metal, having an generation of various free radicals. This study was undertaken to examine the effect of acute cadmium and/or antioxidants on serum lipid metabolism, tissue glutathione, and lipid peroxidation (LPO) levels, and gsherin and metallothionein production in the gastric fundus mucosa. Antioxidants such as vitamin E, vitamin C, and selenium were important for preventing the damage caused by reactive oxygen species.15

**EFFECT OF SELENIUM, ASCORBIC ACID, BETA–CAROTENE, AND ALPHA–TOCOPHEROL**

The aim of this study was to investigate the role of selenium, ascorbic acid, beta–carotene, and alpha–tocopherol on D–Galactosamine (D–GaLN) induced liver injury. D–GaLN is a highly selective hepatotoxin that causes liver injury similar to human viral hepatitis via depletion of uridine nucleotides, which subsequently diminishes synthesis of RNA and proteins. The results suggested that supplementation with the combination of selenium, ascorbic acid, beta–carotene, and alpha–tocopherol may help prevent the development of liver injury.16

**ZINC**

Zinc is an essential trace element for the human organism. It acts like cofactor for the metalloenzymes involved in many cellular processes.17 In developing countries zinc supplementation acts like cofactor for the metalloenzymes involved in many ways. My patients now have adequate protection from wholesome and complete package of antioxidants that is effective of synthetic pool of zinc in the hippocampus. Clinical observations demonstrated serum hypozincemia in depression, which was normalized by effective antidepressant treatment. Moreover, preliminary clinical study demonstrate the benefit of zinc supplementation in antidepressant therapy.20

**REFERENCES**

The POWER-PACKED MULTI-ANTIOXIDANT FORMULA

✓ **LYCOPENE**:
  - Powerful Antioxidant: Evidences suggests that lycopene is a significantly more powerful antioxidant than beta-carotene.
  - Associated with reduced incidence of prostate, digestive tract, breast, lung and cervical cancer, cardiovascular disease and age-related macular degeneration.
  - Helps Increase Male Fertility in Oxidative Stress Mediated Infertility: Prevents against lipid and DNA oxidation Highly concentrated in Testis.  
   (Stahl & Biois Arch Biochem Biophys 1996)

✓ **ALPHATOCOPHEROL**:
  - The most active component of the vitamin E complex.
  - Most powerful antioxidant in the lipid (fat) phase of the human body.
  - Play critical role in protecting against free-radical reaction.

✓ **VITAMIN A**:
  - Acts as antioxidant and prevents blindness.
  - Essential for the integrity of epithelial cells and for cellular growth.

✓ **ZINC**:
  - Acts as an co-factor for a number of enzymes.

✓ **SELENIUM DIOXIDE MONOHYDRATE USP**:
  - Antioxidant and useful in the prevention of cancer and cardiovascular diseases.
  - Prevents cellular degeneration and helps in protein synthesis.

✓ **VITAMIN C (COATED) IP**:
  - Antioxidant and natural antihistamine enhances immunity, shortens the life of cold and is needed in antibody production.

**IDEAL SUPPLEMENTATION FOR**
- In need of Anti-oxidants
- Aging
- Many types of cancer
- Cardiac Disorders
- Osteoporosis
- Male Infertility
- Atherosclerosis and other circulatory diseases
- Arthritis
- Cataract formation
- Senile dementia (Alzheimer type)
- Respiratory diseases induced by pollution