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Glutathione as a Novel Therapeutic Approach to Optimal Health and Wellness

Free Radicals

Free radicals are molecules that contained an unpaired electron. This makes them highly reactive with other molecules. Indeed the two major classes of free radicals produced by the body are called reactive oxygen species and reactive nitrogen species.

Free radicals are both a blessing and a curse. Free radicals are literally the spark of life, playing a critical role in 1) energy production from the foods we eat. No free radicals, no life. 2) Free radicals play a critical role in detoxification since the main means of removing toxins form the body involves adding an oxygen "handle" on toxins in order to remove them more efficiently. 3) They are also essential for a properly functioning immune system, as they are the only weapon the body can make to kill bacteria, yeast, parasites, virally infected or cancerous cells. They are essential for all repair processes in the body since damaged molecules, cells and tissues must first be removed before repair can begin. 4) Free radicals are necessary to transform cholesterol into all of the steroid hormones – thus they are essential for stress adaptation and growth.

Unfortunately, the very properties that make free radicals useful also make them dangerous. Free radicals inadvertently cause ageing. Due to their extreme reactivity, one free radical tends to generate more free radicals in a feed-forward cycle. In any of the processes for which the body uses free radicals – energy release, immune competence, detoxification, and hormone production – the control of free radicals is imperfect. Collateral damage always occurs when the body uses free radicals. Indeed, we now speak of legitimate and illegitimate free radicals depending on whether they serve a useful function in the body or simply cause damage.

Over 600 million years of evolution of using oxygen for energy release, the body has developed some important ways to protect itself from excess free radical production. The first line of defence is enzymatic protection, with three major enzyme systems in place: calatase, super oxide dismutase, and glutathione peroxidase/reductase. Each system is capable of neutralizing specific reactive oxygen or nitrogen species. Even so, these enzyme systems control maybe 70% of free radical protection. The remaining damage needs to be controlled by dietary antioxidants. Early nutritional research suggested that vitamins C and E played

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critical roles as antioxidants, but in the last 30 years, we have discovered that the picture s much more complex. Vitamin C can equally serve as an antioxidant or as a pro-oxidant depending on its availability and the body's needs. Alpha-tocopherol, the species of vitamin E with the greatest antioxidant potential, is now known to function better in a complex with the other 7 variations of tocopherols and tocotrienols. But the most important revision in our understanding of antioxidant protection is the role of colourful compounds found commonly in fruits and vegetables. Many of these compounds are becoming increasingly familiar to nutritional therapists and those who use foods as medicine: anthocyanins, carotenoids, lutein, lycopene, zeaxanthin, sulphoraphanes, anthoxanthins, limonene, phenols, polyphenols, epicatechins, and isoflavones. It is believed that these specific compounds and their ability to quench excess free radicals contribute the health promoting properties of eating colourful fruits and vegetables.

Unfortunately, many people do not consume the levels of fruits and vegetables that they should and their bodies fall back on their last line of defence against free radical damage: endogenous molecules that generally have some other purpose in the body but can serve as antioxidants if absolutely necessary. The only problem here is that once they become oxidize, they can no longer perform their primary functions. These molecules include cholesterol, uric acid, cysteine, glutathione, coenzyme Q10, lipoic acid, nitric oxide, etc. When these molecules are destroyed as antioxidants, the ageing process accelerates exponentially and degenerative diseases become more prevalent.

Glutathione

One molecule stands squarely in the middle of this reduction/oxidation and free radical storm: glutathione. Glutathione is molecule composed of 3 amino acids glycine-cysteine-glutamate. Magnesium and potassium are necessary cofactors for the body to synthesize glutathione. The thiol moiety, or –SH, on the cysteine amino acid at the centre of glutathione is the active site and accounts for its chemical reactivity. Glutathione exists in both reduced (G-SH) and oxidized (GS-SG) states in the body. Glutathione is used in two major biochemical pathways. Glutathione is capable of regenerating any other spent antioxidant via the enzyme glutathione peroxidase (GPx), a selenium dependent enzyme. In doing so, glutathione reacts with another reduced glutathione to form oxidized glutathione (GS-SG). Reduced glutathione can be restored using the sister enzyme glutathione reductase, as long as

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there are adequate body levels of NADPH and FADH, derived from vitamins B3 and B2, respectively.

Individuals with GPx activity below the mean value, and homocysteine levels above mean values have been found to have a >3 fold risk for cardiovascular disease.[1] GPx is especially important in removing lipid peroxides (oxidized fats) from cell membranes.[2] Lipids in membranes are the most frequently damaged molecules from excess free radical activity. Measuring lipid peroxides in the body estimates the whole body oxidative stress and load. Incidentally, in acute oxidative stress (e.g., from toxin exposure) GPx activity increases dramatically. One physical sign of increased oxidative stress and GPx activity is whole body urticaria (itching), and this can be an early warning sign of excess toxicity.[3]

The second major use of glutathione is in detoxification. Glutathione allows the body to detoxify many water-soluble toxins like common solvents, pesticides, and petrochemicals, as well as the most toxic heavy metals mercury, cadmium, and lead. Glutathione also prevents paracetamol toxicity.

Glutathione stands at a cross-road between antioxidant protection and rapid detoxification of water-soluble toxins. Excess utilization of one pathway may strain the efficacy of the other pathway.

Plasma glutathione accounts for only about 1% of total body stores. The rest of the glutathione remains intracellular, where it protects cells from excess oxidative stress, free radical toxicity and toxin exposure. Glutathione can cycle between its reduced form, G-SH, to its oxidized form, GS-SG. Cells use G-SH to maintain intracellular red-ox potential and, if antioxidant capacity is impaired, dump the oxidized glutathione (GS-SG) into the blood stream. Consequently, plasma GSH-to-GSSG ratio is the best available marker for measuring and monitoring intracellular oxidative stress. Incidentally, the best measure of extracellular oxidative stress is the cysteine: cystine ratio. A low GSH/GSSG ratio occurs in a wide variety of diseases, including diabetes, cancer, Alzheimer's disease, Parkinson's disease, ALS, HIV infection, and autism.[4]A low GSH/GSSG ratio has been shown to activate NF-κβ and increase reactive nitrogen species and whole body inflammation[5]

Glutathione is an ideal candidate for preventing excess free radical damage and toxic overload. Unfortunately, 3g of oral glutathione in humans produced no appreciable

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change in the serum levels of reduced glutathione, suggesting it is either digested (hydrolyzed) prior to absorption, or oxidized before absorption.[6]

Recancostat® is a novel formulation of reduced glutathione that is stabilized with a patented anthocyanin complex known as Recyclin. The presence of Recyclin allows the glutathione to be absorbed from the gut and to be absorbed into cells while remaining in its reduced form.[7]

Clinical trials with Recancostat® are many and diverse. In children with allergic asthma, oral Recancostat® therapy led to clinical improvement, to increased interferon-gamma production, improved lymphocyte response to mitogens, increased NK cell activity, and increase in percentage of naive CD4(+) T lymphocytes (refreshment effect).[8] This suggests that supplementation with Recancostat® may provide optimal immune support.

Herpes Simplex Infection decreases intracellular G-SH concentration and serves as a model for many viral infections. Recancostat® efficiently and dose-dependently (5 and 10 mM tested) restored intracellular glutathione in HSV-1 infected cell lines. In mice, Recancostat®, but not un-stabilized glutathione, significantly decreased HSV-1-induced mortality ($P<0.05$). The data suggest that Recancostat® is a suitable antiviral agent against HSV-1 both in vitro and in vivo, indicating that this drug may be of benefit in the adjunctive therapy of HSV-1 or other viral infections.[9]

Recancostat® allowed three separate lines of lymphoma cells to restore normal cell death (apoptosis) by actually lowering intracellular G-SH concentrations in cancerous cells, without any harm to non-cancerous cells.[10]

Recancostat® protects against kidney toxicity in ovarian cancer patients using cisplatin as a chemotherapeutic agent. [11] This study suggests that as an adjunct to chemotherapy, Recancostat® may protect normal cells from the toxicity of the chemotherapeutic agents. More broadly, this suggests that increasing reduced, stabilized glutathione levels may help protect against all forms of chemical toxicity, and not just by protecting against direct chemical toxicity but also protecting from the oxidative damage that such detoxification may incur.

Oral Recancostat® therapy has been shown to increase levels of reduced glutathione in the body. Increased body levels of reduced glutathione protect us from ubiquitous free radical damage and the damage that may be caused by water-soluble toxins like

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solvents, pesticides and heavy metals. The Scave® line of supplements Scave®Sportiv, Scave®1Forte, and Neuro®Scave, provide safe and effective daily doses of Recancostat® in proprietary blends of supportive essential nutrients for optimal health and wellness.

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