The Whey to Enhancing Glutathione, Our Most Powerful Endogenous Antioxidant and Detoxifier

Glutathione is widely found in all forms of life and plays an essential role in the health of organisms, particularly aerobic ones. In humans, animals, and plants, glutathione is the predominant non-protein *sulfhydryl group* and functions most especially as an antioxidant, keeping its own -SH groups and related proteins in a reduced (non-oxidized) condition. [1, 2]

Though there are undoubtedly multiple functions for glutathione yet to be appreciated we do know that glutathione is:

- a co-factor for the *glutathione peroxidases*, which are crucial selenium-containing antioxidant enzymes.
- a co-factor for *glutathione S-transferases*, enzymes which are involved in the detoxification of *xenobiotics*, including carcinogens.
- involved in the regeneration of ascorbate (Vitamin C) from its oxidized form, d*ehydro-ascorbate*. [3]

Glutathione itself is a non-essential nutrient composed of three amino acids: *glutamic acid*, *glycine* and *cysteine*, or more exactly the tripeptide *L-gamma-glutamyl-L-cysteinylglycine*. Availability of cysteine is a limiting factor in the liver's synthesis of glutathione.

Chronic functional glutathione deficiency is associated with immune disorders, an increased incidence of cancer, and in the case of HIV disease, probably accelerated pathogenesis of the disease.[4, 5]

Acute manifestations of functional glutathione deficiency can be seen in those who have taken an over-dosage of acetaminophen (Tylenol). A vital role of glutathione is the maintenance of a normal redox state of the liver. An overdose of acetaminophen leads to its metabolism into large quantities of N-acetyl-benzo-quinoneimine (NABQI) in the liver. NABQI depletes hepatic glutathione stores, placing an enormous oxidative stress on the liver, leading to liver failure.[6]

N-acetyl-L-cysteine

N-acetyl-L-cysteine (NAC) is integral to the treatment of acetaminophen overdose. This is due mainly to its ability to regenerate liver stores of glutathione. NAC is a bioavailable delivery form of L-cysteine, which serves as a major precursor to the antioxidant glutathione, but its half life is only 30 minutes. [7, 8] Therefore its use as a supplement to enhance glutathione levels is limited.

Alpha Lipoic Acid

Alpha-lipoic acid (ALA), which is synthesized in mitochondria and also requires L-cysteine, appears to participate in the recycling of glutathione.[9] There is extensive animal work showing that lipoic acid, by supporting glutathione levels, can exert significant

protective effects against oxidant damage related to ischemia-reperfusion injury.[10] More research may be needed to further elucidate these mechanisms and determine whether these results will apply in humans.

Reduced Glutathione

Glutathione as such is present in the diet in amounts usually less than 100 milligrams daily. It does not appear that much of the oral intake is absorbed from the intestine into the blood, at least in humans. However, there is an occasional study that does show an increase in circulating glutathione after oral administration of reduced glutathione.[11, 12, 13, 14] There is greater evidence that glutathione may be absorbed into the *enterocytes* where it may help repair damaged cells.[15] Patents have been submitted for reduced glutathione in a *liposome* claiming enhanced absorption.[16]

Organic L-Selenomethionine

Glutathione formation requires an adequate level of *selenium.* Selenium belongs to the sulfur group of elements which includes oxygen, tellurium and polonium. It is an essential trace element in human and animal nutrition. *L-selenomethionine* or *L-selenocysteine* are *selenoproteins* necessary to the endogenous production of glutathione peroxidases (GSHPx 1-4).[17, 18]

There appears to be an inverse relationship between coronary heart disease and selenium intake. The possible anti-atherogenic activity of selenium may be accounted for, in part, by its antioxidant activity. Glutathione peroxidase may protect low density lipoprotein (LDL) from oxidation, thereby inhibiting atherogenesis and platlet aggregation. (*Lipoperoxides* impair *prostacyclin* synthesis and promote *thromboxane* synthesis).[19]

Undenatured Whey Protein and Colostrum

Undenatured whey and colostrum proteins' antioxidant, detoxication and immunological effects are in no small part likely related to the *glutamylcysteine* groups which act as the substrate for *glutathione* (GSH) synthesis. These *cystine* groups needed for the intracellular conversion to *cysteine* are in whey and colostral sub-fractions.[20] However, this highly bioavailable, double bonded cystine portion is very thermo-labile. *Denaturization* by heat will therefore greatly inhibit the ability of whey proteins to act as precursors to GSH synthesis, though not affecting the biological value (BV) of whey as a protein nutrient as such.[21]

Conclusions

Reduced glutathione is the major endogenous antioxidant and detoxication peptide. Its hepatic production and intracellular levels may be enhanced in the following ways:

- NAC, 200 mg, 3 or 4 times daily
- Reduced Glutathione, in liposome: 50 - 200 mg, once or twice daily

- Selenium, which is abundant in garlic, onion, broccoli, whole grains and most especially Brazil nuts, has an optimal daily dosage at perhaps 200 mcg a day.[22]
- Whey Protein, undenatured, 10-15 gm, 1 to 3 times a day
- Colostrum, whole, 2 gm, 1 – 3 times a day.

A palatable functional food formula of undenatured whey and/or colostrum, combined with some of the above nutraceuticals, may be both the most clinically efficacious and nutritionally complete way to enhance endogenous glutathione production.

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6) PDRhealth.com, NAC, www.pdrhealth.com/drug_info/nmdrugprofiles/nutsupdrugs/ace_0178.shtml

7) Exner R, Wessner B, Manhart N, Roth E. Therapeutic potential of glutathione. Wien Klin Wochenschr. 2000; 112:610-616.

8) Ibid., 6

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