DISCOVERIES IN CANCER TREATMENT

Biochemical Significance of the Vitaletheine Modulators in Conventional Oncology Treatment Protocols

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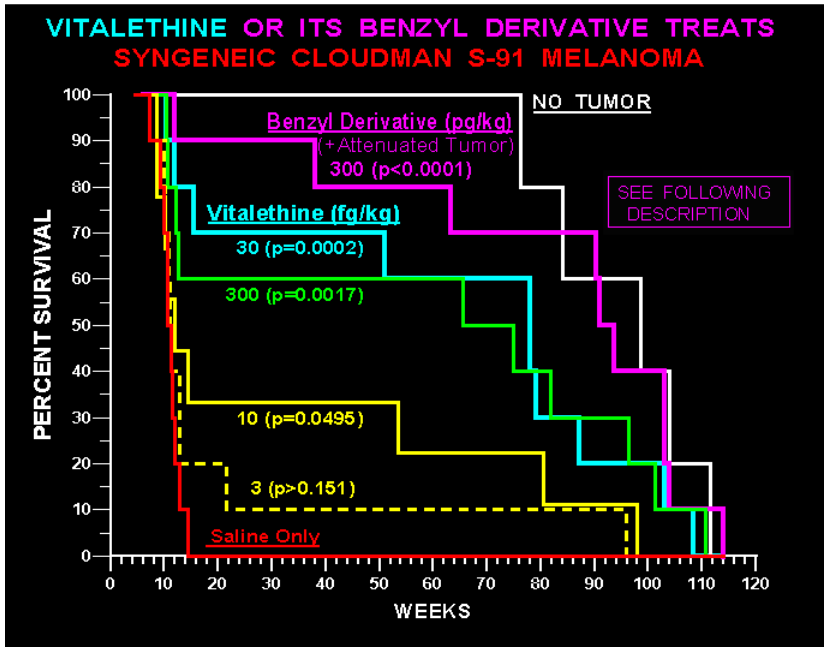
Introduction

An article in the Journal of Clinical Oncology reported a study revealing that, as cancer incidence rates increase, oncologists have become increasingly aware of their patient's use of alternative medicine. Although few patients abandon conventional care, some 60 to 80% combine complementary alternative medicine with conventional treatment. The article further suggests that physicians willing to communicate openly in a nonjudgmental style about complementary medicine may avoid disrupting the patient-provider relationship and possibly encourage compliance with conventional treatment. In concluding, the authors encouraged the oncology community to improve patient-provider communication, offer reliable information to patients, and initiate research on possible drug-herb-vitamin interactions.[1]

Vitalethine and Its Importance To Clinical Oncology?

Vitalethine is a naturally occurring chemical component in mammals that is "vital" to healthy immune function. Laboratory researchers discovered a related family of compounds called the *Vitaletheine Modulators* and demonstrated therapeutic control over cancer during animal studies supported in part by grants from the National Institutes of Health. Clinical trials on humans are being structured at prestigious medical research institutes.



Initial response rates of at least 90% were reported by two back-to-back articles in *Cancer Research*.[2,3] Of laboratory mice injected with uniformly fatal melanoma and treated with

un-optimized regimens of the Vitaletheine Modulators, 70% survived for normal lifetimes. Importantly, 100% survival rates were reported in mice with particularly aggressive myeloma.

All current data indicate that the humoral immune system is largely responsible for therapeutic responses in mice study models, an antibody-mediated process that can be absolutely dependent upon Vitalethine.[2] Human and mouse spleen leukocyte responses are virtually identical when using compounds structurally related to Vitalethine.[3] Thus, similar human responses can be anticipated from the animal studies.

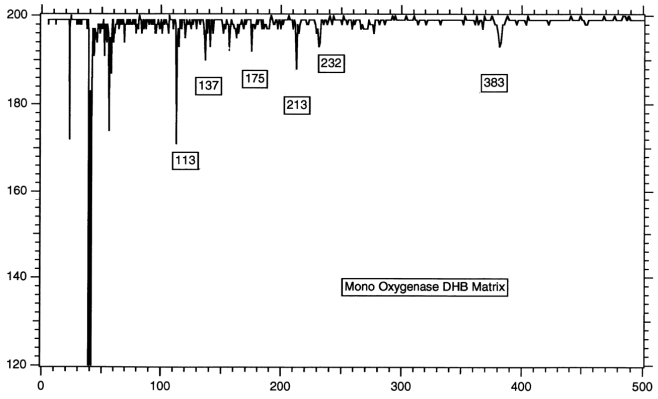
Technical Description

Known to control enzymes and body chemistry for more than 70 years, sulfur compounds such as the disulfide, cystamine ($H_2NCH_2CH_2SSCH_2CH_2NH_2$), influence regulation of sugar metabolism by magnesium and manganese ions. Thus, metabolic pathways that break down, produce, and store sugar are coordinately regulated at each key step by sulfur chemistry, enabling the controlled use of sugar and starches for energy. Thyroid hormones[4] and the body's production of steroid hormones from cholesterol also are regulated by the body's sulfur biochemistry. Sulfur chemistry even regulates cell division in the body, a process that runs amuck in tumors and cancers and is favored by a reducing (*e.g.* thiol-rich) environment. A certain amount of cell division, for example producing red blood cells that carry critical oxygen to the rest of the body, must be carefully maintained to replace cells that naturally die off. Indeed, Otto H. Warburg received the Nobel Prize for medicine in 1931 for showing that cells tend to lose control and become cancerous when deprived of oxygen carried by these very same red blood cells to produce a thiol-rich environment.

The mechanisms for regulation of these metabolic pathways remained a mystery until the discovery of the Vitaletheine Modulators. Since fragments of this natural disulfide, such as the other disulfides beta-alethine and cystamine, and even the amino acid, beta-alanine, exhibit traces of the same biological activities, clues to Vitalethine's existence have been known for some time. Vitalethine, in its synthetic disulfide (VSSV) form, and especially when reduced to its thiol form (2 VSSV --> 4 VSH) and polymerized (Vitaletheine V_4) [2], increases the production of red blood cells that carry oxygen throughout the tissues of the body. Vitalethine and other members in this family of Vitaletheine Modulators were found to stop melanoma and myeloma, while producing antibodies capable of rupturing "foreign" or "aberrant" cells, such as pathogenic, infectious agents and intractable cancer cells. Responses to un-optimized treatments with the Vitaletheine Modulators often occur at phenomenally low concentrations, as little as 3 attograms (1×10^{-18} grams)/ml in cell culture or 3 femtograms (1×10^{-15} grams)/kg body weight.[2] Scientists have been shocked at how a molecule as simple as Vitalethine could have such potent and profound effects in balancing various body chemistries.

Vitalethine is made in the mammalian body from i) the amino acid, L-cysteine, or its disulfide, L-cystine, found in the more nutritious proteins (*e.g.*, bison round or oat bran), and ii) vitamin B_5 (D-pantothenic acid)[2] found abundantly in royal jelly and rice bran. Thus, when regulation of cell division fails, proper sulfur chemistry can enhance production of antibodies that rupture and kill cancer cells, a capability that is critical when they are irretrievably out of control.

Furthermore, when cancer cells divide, substantially more cholesterol is needed to stabilize membranes of the two resulting cancer cells. When cholesterol is limited, the membranes of cancer cells become brittle instead of fluid, causing them to rupture and die naturally (apoptosis). Significantly, beta-sitosterol, a plant sterol that blocks cholesterol, is present in many herbs reported to have therapeutic benefits in cancer. Also helping to block cancer genes and to make cancer cells more fragile and prone to die naturally is an "oxygen-requiring" enzyme that chokes off the synthesis and action of small isoprenyl molecules, which turn on cancer genes (like *ras*) and build cholesterol. A completely pure preparation of this "monooxygenase" has a molecule on it that is the same size (M+=383) as expected in the mass spectrometer for Vitalethine. Thus, this "enzyme" with Vitalethine indirectly catalyzes the oxidation of cysteine residues in enzymes, proteins and peptides to disulfides, sulfenyl iodides, and sulfenic acids, and to mixed disulfides with other small molecular-weight thiols, providing a vast array of regulation for virtually every biochemical pathway in the body.

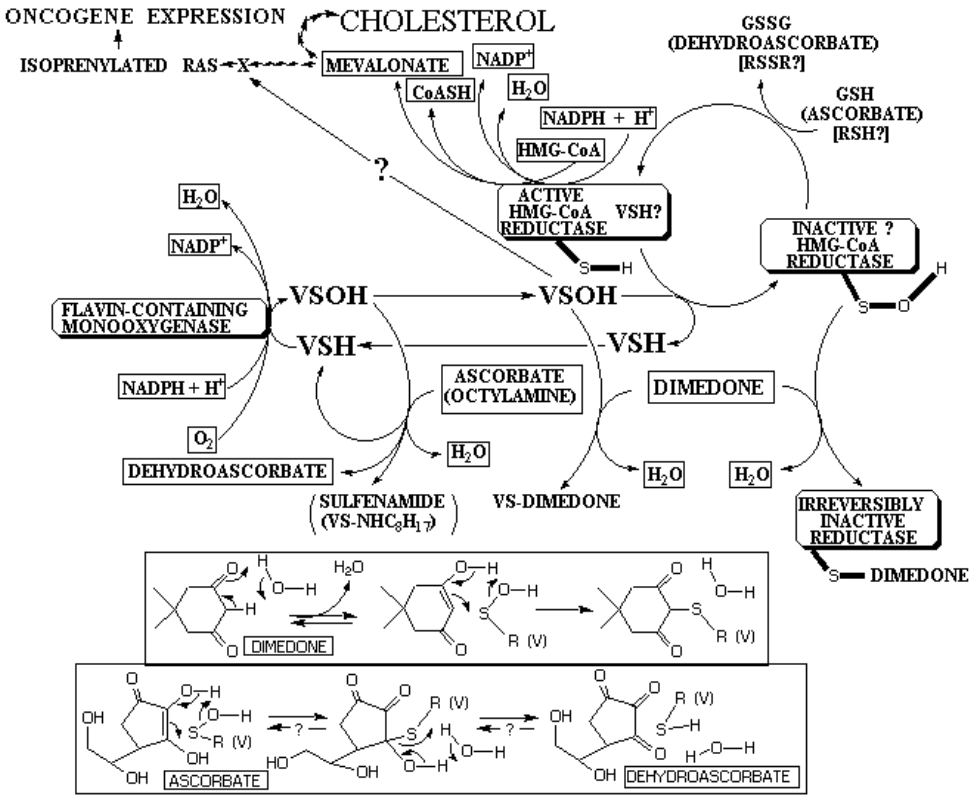


Significantly, the scientific literature reports cancer patients often are deficient in critical B vitamins. This "oxygen-requiring" monooxygenase uses these B vitamins to "oxidize" cysteamine (CSH-->CSSC) or Vitaletheine (VSH-->VSOH). Therefore, without essential B vitamins and other nutritional factors needed for this enzyme to function properly, regulatory oxidation fails, and reduced (thiol) forms such as cysteamine (CSH) and Vitaletheine (VSH) accumulate. In addition to stimulating division of cancer cells, accumulations of thiols such as cysteamine (CSH) are known to cause single-strand breaks in DNA[5], increasing the likelihood that genetic mutations, like those observed in advanced and intractable cancers, will occur. It is important to note, however, that only 3 to 10% of cancers are thought to result from familial causes (including inherited genes). Thus, the vast majority of cancers obviously are attributable to nutritional deficiencies, exposure to environmental toxins, or both.

Unfortunately, these "beneficial regulatory oxidations" can be blocked by high doses of "reducing" vitamin C [SEE *Monoxygenase Control of HMG-CoA Reductase and Oncogenic Expression* below]. Similarly most, if not all, carcinogens are known to block i) sulfur compounds like the Vitaletheine Modulators, ii) their monooxygenase receptor(s), or iii) factors needed for proper functioning of critical "sulfur-regulation" [SEE *Environmental Factors Affecting the Vitaletheine Modulator/ Monooxygenase System, infra*, as updated at http://www.vitaletherapeutics.org/vtlcsmal.htm].

Monooxygenase Control of HMG-CoA Reductase and Oncogenic Expression

The relationship between monooxygenases and HMG-CoA reductase is important for several reasons. First of all, enzymes catalyzing the oxidations of thiols control cancer. The majority of cancers are dependent upon the isoprenylation of *ras*, the monooxygenase blocking both the reductase step producing the isoprenyl (mevalonate) units and the later actual isoprenylation of *ras* by modifying (oxidizing) the cysteine residues of *ras* that would otherwise be isoprenylated. By decreasing HMG-CoA reductase activity and the production of mevalonate, monooxygenase activity also can control the biosynthesis of excess cholesterol, a suspected factor in heart disease.



Sulfur metabolism's improvement of risk factors for heart disease was independently observed; whether supplied as free amino acids or in dietary protein, a significant decrease in cholesterol and LDL, an increase in HDL (the good cholesterol), and a decrease in triglycerides were observed

when rats were fed high cholesterol diets enriched with cysteine/cystine.[6] Since cysteine is not a substrate for the monooxygenase, in order for cysteine to work in this regulatory pathway it must first be decarboxylated via the Coenzyme A pathway, which includes precursors of the Vitaletheine Modulator family of compounds.[2] Recall that D-Pantothenic acid (vitamin B_5) is also used in this pathway as a building block for the Vitaletheine Modulators.

Individuals suffering from cystinosis or some types of kidney stones probably should be cautious about supplementing their diets with L-cystine or L-cysteine. Of the two, L-cystine is absorbed more slowly and less completely, making it safer. There are indications that D-Pantothenic acid supplements alone may benefit this health problem by helping to metabolize the accumulating L-cysteine and L-cystine. Additionally, L-cystine is safer because it is less likely than L-cysteine (especially its HCl salt) to extract carcinogenic metals from any stainless steel processing equipment used to prepare the supplement. The body can convert L-cystine to L-cysteine by reduction. The resulting "cysteine" (*alias* the "reduced", thiol, CYSH, or sulfhydryl form) provides protection against aflatoxin and other carcinogenic and toxic mycotoxins, that contaminate our food supply, by reacting with them before their absorption. However, "cysteine" probably also requires "auto-oxidation" to its sulfenic acid (CYSOH) before some of this benefit is realized, thereby explaining both the low rates at which aflatoxin is neutralized with "cysteine" and why cysteine is slowly depleted from our food supply by contaminating mycotoxins.

Since the monooxygenase is unstable in the absence of NADPH and NADP+, a deficiency of niacin (from which these cofactors are made) may be particularly disruptive to this enzyme and its ability to block HMG-CoA reductase. Also, if results in the "test tube" are any indication, the absence of oxygen should lead to dramatic losses of the monooxygenase when NADPH is adequate. In other words, under hypoxic (or low oxygen) conditions thought to exist in the center of rapidly growing tumors, NADPH may aggravate regulatory problems due to the loss of monooxygenase activity while still directly favoring activities of HMG-CoA reductase. When excessive, this unregulated mevalonate synthesis can contribute to heart disease (high cholesterol and stenosis) and to tumor proliferation (isoprenylation reactions).

These relationships provide rational explanations for two previously puzzling phenomena:

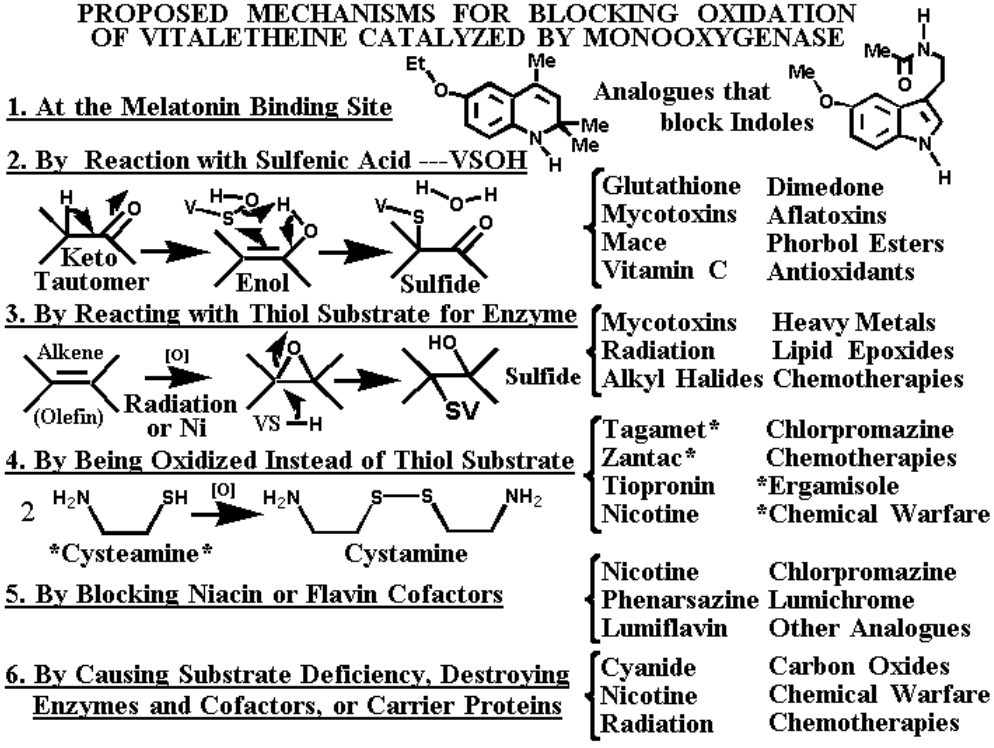
- Depriving tumor cells of oxygen in culture is known to make them more malignant (intractable) when inoculated into laboratory animals.
- Despite the fact that niacin is used to make the NADPH cofactor for the reductase, this vitamin is better known for its ability with oxygen to lower, not increase, cholesterol.

With these considerations niacin should be most useful in the prevention of cancer and heart disease, especially in tobacco users since the nicotinamide version probably offsets the carcinogenic potential of demethylated nicotine metabolites. If rapid tumor growth can be controlled by other

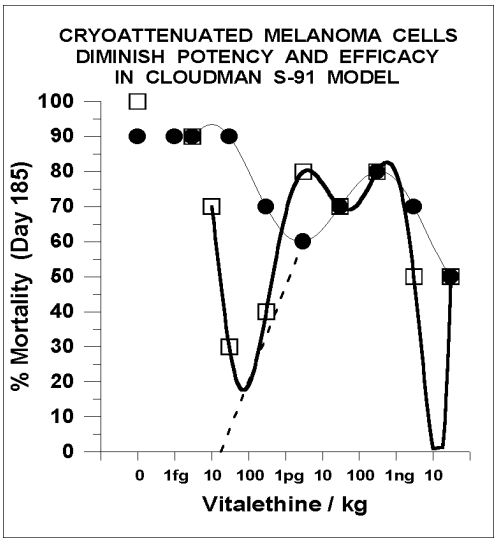
means and if the tumor tissue can be adequately oxygenated, nicotinamide may have therapeutic value even in large tumors. There is guarded therapeutic potential in advanced heart disease, as well. Arteries occluded by proliferation of the endothelium, as with rapidly growing large tumors, outstrip the oxygenated blood supply. Since these are similarly-linked difficulties of pathological proliferation and poor aeration of tissues in these two diseases, several complementary therapies supporting the Vitaletheine Modulators are of interest. These therapies include hyperbaric oxygen, nutritionally enhanced genetic expression of the monooxygenase in poorly oxygenated tissues, proliferation-suppressing agents that have a sparing effect upon the revascularization, and re-oxygenation of tissues.

Environmental Factors Affecting the Vitaletheine Modulator/Monooxygenase System

- Nutritional Deficiencies--*such as Cysteine and Pantothenic Acid*
- Savvy Cheese--*a guide compiled from a US Department of Agriculture database*
- Light Pollution--*and Exposure to Ultraviolet and other Forms of Radiation*
- Aflatoxins and Mycotoxins--*in our Food and Related Chemical Toxins*
- Toxic Metals--*such as Lead, Cadmium, Mercury, Bismuth, Plutonium, etc.*
- Arsenicals--*such as Phenarsazine used in "Pressure-treated" Lumber*
- Chemical Warfare Agents--*such as Phosgene, Sarin, HN1, Lewisite 1, Mace, Mustard Gas, Soman, Tabun, and VX*
- Key Pathways--*Regulated by Monooxygenase and Vitaletheine Modulators*
- Triclosan Toxicity--*to Thyroid Hormone Metabolism (Wilson's Syndrome?)*



It has been determined that a variety of toxins probably poison the ability of the Vitaletheine Modulators to prevent and treat cancer. Most notably among these toxins are the dead cancer cells, themselves. Conventional chemotherapy and radiation kill and leave tumors, *in situ*, to be re-absorbed, releasing the carcinogenic substances that caused the cancer to again produce "metastases" when these toxins accumulate elsewhere in the body. Furthermore, as cancer cells die, rupture and lose their intracellular antioxidants, membrane fragments oxidize according to reaction #3., *supra*, and poison the very Vitaletheine Modulator-dependent (VSH) immune system that normally would have prevented and treated the cancer. This is graphically illustrated by the following figure in which the therapeutic response to Vitalethine (open squares) is attenuated by the co-administration of dead cancer cells (filled circles):



Note that the extrapolated efficacy in the presence of dead cancer cells drops from approximately 80% survival to only about 40% survival with the co-administration of only a tiny bolus of attenuated tumor cells. From this data, a completely effective therapeutic window for Vitalethine can be crudely extrapolated (dotted line) at about 10 fg/kg or less, a situation that would reflect a theoretical complete absence of environmental toxins and dead cancer cells. Since this amount of Vitalethine is flanked on either side by the amounts of plutonium and aflatoxins that poison sulfur chemistry and cause cancer, this is the range of Vitalethine concentrations thought to be available naturally when the body is well-nourished and free of such environmental toxins.

Thus, insights gained in the discovery of the Vitaletheine Modulators set the stage for exciting new developments in the fields of environmental toxicology, nutrition, and in the prevention and treatment of a variety of supposedly intractable and incurable diseases, such as cancer and heart disease.

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