

The Molecular Biology of How Dietary Supplements Support Optimal Human Health

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This manuscript has been assembled to present findings that are believed to build a case that further and more formal evaluations are justified in regard to the role played by micronutrients in avoiding disease, maintaining and supporting health. This investigator has been a member of an investigative team formed in the 1980s that was composed of veterinarians, Ph.D.s, physicians and other basic scientists or special-niche trained professionals that have been progressively evaluating micronutrients. Despite initial skepticism on the part of each research participant, it is now believed that pilot studies demonstrate that special dietary supplements that replace micronutrients low or missing in the modern, urbanized food chain are worthy of more formal research. This position comes from a growing body of evidence-based observations that need to be more critically examined and quantified. Unfortunately, this is a very expensive process. Significant progress has been achieved in the dietary supplement field during the two decades since our investigative team was assembled.

Research was initially funded to develop a new drug from an unidentified plant synthesized compound in the leaf gel of the aloe vera desert lily. In due time the active ingredient in aloe leaf gel was found to be a micronutrient. More specifically it is a glyconutrient (Glycos-Greek for sweet or sugar) in that the active component in aloe is chains of mannose sugars. The next step was to recognize that mannose is used in the cellular synthesis of bioactive structure/function compounds. These compounds are synthesized under gene control to conduct innate host defense, repair, healing, to maintain homeostasis and conduct virtually all processes recognized as life. This is why the use of aloe gel to support health dates back to more than 5,000 years. This opened our eyes to the fact that there are other glyconutrients and essential micronutrients that are low, absent or destroyed due to green-harvest, highly processed, environment debased and over-cooked food. There are phytonutrients maximally synthesized in plant cells when the fruit and vegetables are allowed to plant ripen, that include a vast array of free radical scavengers, anti-oxidants, and micronutrients of various molecular species. These plant sourced micronutrients are denatured by exposure to the 21% oxygen in air, exposed to heat and exposed to extremes in acid/alkali or pH. In addition, the micronutrients include phytogenins that are plant-synthesized sterols in certain legumes and tubers, and often rare trace elements missing in the modern food chain that are required to support cellular assembly of glycoproteins and glycolipids and are incorporated into the structure of enzymes active in cellular synthesis.

The first serious challenge to establishment medical therapeutic thought and practice is that too many favorable things happen when the same combination of micronutrients are added to the diet of individuals with compromised health. One must first comprehend that the micronutrients constitute a milieu of hundreds and possibly thousands of molecular species and elements that are used by cells in the complex biochemistry that conducts life. The cells are provided a nutrient pool by dietary supplementation from which nutrient molecules are available, as required, to cope with and balance metabolic alternations caused by environmental stresses encountered by the trillions of cells in a human body. Such adaptations are sensed at the cellular

level and responded to by activation of genes that transcribe the messenger ribonucleic acid (mRNA) that provides the coded instructions for proper synthesis of compounds required to maintain, regulate, or restore systems within cells and tissues to a “normal state” or “zone of good health.” Maintaining the normal status is the goal of the biochemistry as was first noted by the monumental research of the French physiologist Claude Bernard, Ph.D. The healthy state cannot be maintained or restored if the elements and nutrient molecular units, or micronutrients, are not available for proper synthesis of communication molecules that carry coded-instructions between cells that assemble structure/function compounds that constantly cope with the stresses of life. Such compounds restore balance within cells and return the body to a “normal state of structure and function” that is experienced in daily living as being healthy.

Importantly, supporting natural biochemical process with more complete nutrition to optimize production of structure and function compounds by the human body’s cells is not the treatment, mitigation or cure of disease. For a fact, we have seen that cancer cells in culture grow better when micronutrients are added to the nutrient medium. The defense systems of the host that are controlled by genes must take the nutrients and element units and join them together to assemble and form bioactive compounds that are designed to detect and destroy abnormal cells. There is no bioactivity until the body uses the nutrients to make substances that act to bring the body back into the normal-zone termed homeostasis. When homeostasis is achieved, this status is experienced in daily living as good health, wellness or well being. This healthy status is the condition optimal nutrition supports. **The biochemical mechanisms to be shown apply to all nutrients and elements required by the genetic instructions that control cellular synthesis of structure and function compounds that become bioactive and conduct life.** Our team’s research was focused on glyconutrients and this is emphasized. However, the use of sugars in cellular synthesis is a model for utilization as units that are assembled to make bioactive compounds that span the use of amino acids, lipids (fats), numerous elements, micronutrients, carbohydrates and vitamins.

The membranes within and surrounding cells are dynamic, incredibly complex units of structure and function. Oversimplified, these membranes determine what goes in and comes out and the rate of such activity for all cells and retain within the cell the sub-microscopic organelles present inside the various types of cells in various organs. Cellular membranes are also synthesized on the bio-assembly line in cells that require a molecular nutrient supply to be able to be made structurally correct and thus function properly. **The molecular structure of a bioactive compound determines its function.** The major supply of components for producing bioactive compounds that conduct the biochemistry of living cells is supplied in the diet. Dietary content and choices made are much more important for human health management than is currently recognized by most professionals and the public.

It is a grievous error that creates vast errors in western society that an emphasis for health management is based on faith in drugs that are largely chemical poisons elevated by requirements of a government agency to the status of expensive prescription drugs. The mode of action of such drugs is to interfere with the engineering and design of life as is manifested in biochemistry and physiology to reduce symptoms. This essay is to advocate using nutrition is the first action to be taken that supports the manner that the human body works by providing what the genes (coded instructions for conducting life) require to assemble the structure/function

compounds that correct deviations from the status of “normal”. The benefits to the individual and society is that a nutritional approach is non-toxic and safe beyond comparison, effective to the point it exceeds professional and common societal belief and is without equal for being economical. **Nutrition supports the engineering and design of life as coded in the genes to conduct the chemistry of life.**

To the casual observer, when health is restored by providing nutrients the cells require for synthesis of cell activating molecules termed cytokines (Greek. cyto-cell, kine-activation), it appears that an active, interventional treatment of disease was initiated. That is not the reality for the activity that has been successfully conducted. Roger Williams, Ph.D., pioneer nutritional researcher, best described this non-pharmaceutical natural phenomenon. In his most important book, *Nutrition Against Disease*,¹ 1971, Dr. Williams states that the theme of his life’s work and all his many books on nutrition is captured in the statement,

“The human body heals itself and nutrition provides the resources to accomplish the task.”

The language of the Dietary Supplement Health and Education Act of 1994 (DSHEA) codifies in legislation and the pilot scientific observations in this monograph validate and support Dr. William’s insight, understanding, and decades of pioneering research on nutrition. Elements and nutrients do nothing until the cells under control of instructions coded in the genes assemble bioactive compounds to carry out the functions of life stored much like a dynamic library in the nucleic acids (DNA) of the genes.

Unfortunately, medical education gives very little time or attention to nutrition. Therefore, the viewpoint that explains the benefits revealed in the series of papers our research team developed requires a re-education for health care professionals. A number of fundamental principles are required for comprehension to grasp the full importance of the power of nutrition to support health, prevent disease and restore health. The most basic is an illustration Dr. Williams used in the above cited book. He describes a chain on a table-top in a coiled-pattern. At just over three-quarters of a turn the chain rises from the table-top in the center to make a form like a snake ready to strike. Each chain-link is described as representing a nutrient or element required for cellular synthesis of bioactive structure/function compounds. If all the links or nutrient units are present, the nutrient supply coil can rise supported by the other links to represent the state of well being and good health. However, if any element or nutrient, those identified and even those yet to be discovered, the compromised state fits into an established pattern that is artificially, for communication purposes, classified as a diseases. The link at the point the chain rises from the surface is described as being the missing nutrient or element, and when absent the chain falls to the table top to symbolize this nutrient deficiency state. Furthermore, Dr. Williams stated that the state of well being cannot be restored until the missing nutrient is supplied. Those familiar with pure iron deficiency anemia have observed the practical validity of this narrow and well defined illustration.

For various reasons in the nutritional support of health the actions taken and communication should be a quest to restore the status of wellness and a high quality of life. Disease terms should be avoided due to professional limitations deemed the practice of medicine and

government agency regulations that penalize any individual or company that strays into using disease terms.

My professional deviation from the standard medical orientation that health is restored only by surgery, drugs, radiation, major life style changes and avoiding risk laden activity began with joining a research team in 1985 that was seeking to determine why human beings have used aloe vera leaf gel for over 5,000 years. This project was financed by investors interested in financing the discovery of a new expensive and high profitable drug. A labile white powder in the leaf gel was stabilized and extracted from the plant tissues. This material was eventually determined to be chains of mannose sugars hooked together in variable lengths, or numerous molecular weights. A great amount of time and money was expended trying to make a medication of this substance. The aloe polymannose was shown to support the natural biochemical mechanisms that conduct innate activity of cells that was antiviral², antibacterial³, anti-neoplastic⁴, healing⁵, and to function for supporting intracellular stability, balance, and adaptation in stressed cells⁶ (increasing the synthesis of reduced-glutathione, the principle intracellular anti-oxidant and multi-systems balancing compound) animal models⁷, and human subjects.⁸

Entering the new drug approval process, the first difficulty in Food and Drug Administration (FDA) required evaluations of a new pharmaceutical agent was that no toxicity could be elicited by massive amounts of the aloe polymannose in multiple animal models and humans.^{9,10,11} This is not expected nor do the regulations for a proposed new drug take into consideration such a finding. The Father of Pharmacology, Paracelsus, stated, "All drugs are poisons, the benefit depends on the dose." This reality for chemicals elevated to the status of an approved drug has not changed in 500 years. The laws of various nations conform to this known characteristic of pharmaceutical agents. The drug laws before 1994 made no concession for a non-toxic substance, even nutrients that have a health supporting property. The second problem encountered with agency premises and practices was that too many desirable responses of improved health, a higher state of wellness, were fostered by the addition of the complex sugar of aloe leaf gel source to the biochemistry of an animal or human. There is a serious dictum in medicine, "There are no panaceas." This position is taken to heart along with the common sense mantra, "If it appears too good to be true, it is not true." The wide spectrum of desirable health-promoting activities fostered by use of this non-toxic complex sugar exceeded any substance on record and the FDA is not organized for, nor receptive to evaluate multiple benefit-producing substances. This agency is set up to conduct evaluations for a new drug that will be given a single-use or indication label claim. The medical profession is not prepared to entertain the reality that on giving one substance for a symptom or disease that other health compromises will improve. Additional symptoms of toxicity and side-effects are more common, expected and consistently fulfilled when pharmaceutical drugs are administered to sick people.

Eventually, the capacity of the glyconutrient polymannose when consumed for an acute or chronic infection was accompanied by other health challenges that improved or faded away, like asthma, migraine headaches, arthritis, skin problems and autoimmune conditions. **This phenomenon has been termed the "White Box" side-effects.** Furthermore, those oriented in standard medical care cannot readily assimilate nor accept such a heretical challenge to unquestioned dogma long established in the attitudes of a professional priesthood that follows a catechism of evidence-based science. To attain such evidence, the drug is to be as pure and

totally defined as possible. Multiple heterogeneous molecular species within a natural nutrient formulation, with multiple active moieties that interact and provide synergy in unknown ways, as found in nature, is an anathema to medicinal developers, regulators and a physician's orientation. Nutrition does not fit into the drug paradigm for a mechanism of direct action for intervention or the philosophy of purity, being a defined, if not a single molecular species, as far as possible. In the fundamentalist religion of medicine, nutrition is "sinful" in its content and ill-defined, broad manner of providing non-toxic and economical health benefits. The paramount transgression as seen in professional and institutional responses is that nutrition and other natural modalities threaten the profitability of the sickness industry. Correcting or preventing the structure/function alteration by natural means prevents the need for multiple drug prescriptions, hospitalizations, treatments, office visits and diagnostic studies. This is a major threat to the sickness industry and its research foundations based upon and supported by the lack of their being a cure for a disease upon which grants are issued and careers are built. Finding a cure could result is a disaster for a professional team of investigators conducting medical research and to drug companies seeking constantly rising sales and profitability.

To move forward into wide human usage required federal legislative action. The new legislation's preamble created a new paradigm and regulatory niche into which the health-promoting glyconutrient polymannose isolated from the aloe plant gel could fit. The Dietary Supplement Health and Education Act of 1994 (DSHEA) made it possible that this trace micronutrient could fit in a regulatory category of a dietary supplement. With this step aloe polymannose could be classified and regulated by government monitors of health products and thus marketed. No claims to treat or cure disease are permitted for herbs or dietary supplements that fit into the DSHEA legislation and regulations.

Another important event was contained in a review published in 1985 by a pair of biochemists Stuart and Rosalind Kornfeld.¹² In this paper a step-by-step bio-assembly line within all young cells and fully functioning cells is described. Most importantly, it is revealed that in the endoplasmic reticulum, during the second major step in biosynthesis in all cells, nine molecules of mannose are required to initiate assembly of glycoproteins and glycolipids. This stimulated recognition that the active principle, the sugar mannose, isolated from the aloe gel where the plant had synthesized the monosaccharide and polymerized it into long chains, was utilized for cellular synthesis in this organelle within human cells. Thus, the biochemistry and electron microscopy of why human beings have used aloe vera since the advent of recorded history was scientifically described by our research team. That is why the white powder, a monosaccharide i.e. a sugar, had relatively no toxicity or side effects. Its mode of action was not like a drug because it is a micronutrient, a glyconutrient to be exact, utilized in the molecular assembly within cells to start the synthesis of structure/function molecules. The complex polysaccharide meets the non-pharmaceutical regulatory requirements demanded to warrant an exemption status in DSHEA regulations for a dietary supplement. This mechanism of action further solidifies the premise that supplying a dietary supplement of this nature is not the treatment of disease. Nutritional support of instructions coded in genes that are programs for normal physiology is operational. Such instructional programs in genes require nutrient molecules to make it possible to completely and correctly assemble structure/function bioactive compounds made by the cells and thus optimize health. Importantly, not only is this not a biochemical mechanism of treatment or cure, one must not indicate by word or print that it is a therapeutic intervention meant to

restore health or prevent disease. Wellness and quality of life are supported and is the terminology to be used. The FDA adheres to the position that to claim any substance improves health converts it to the status of being a drug. At this point stating that a nutrient or element supports health through more optimized nutrition is believed to avoid such a pitfall. The sickness industry's monopoly extends into influence in the government and control of our language to the point it commands exclusive use of specific words in the nation's vocabulary.

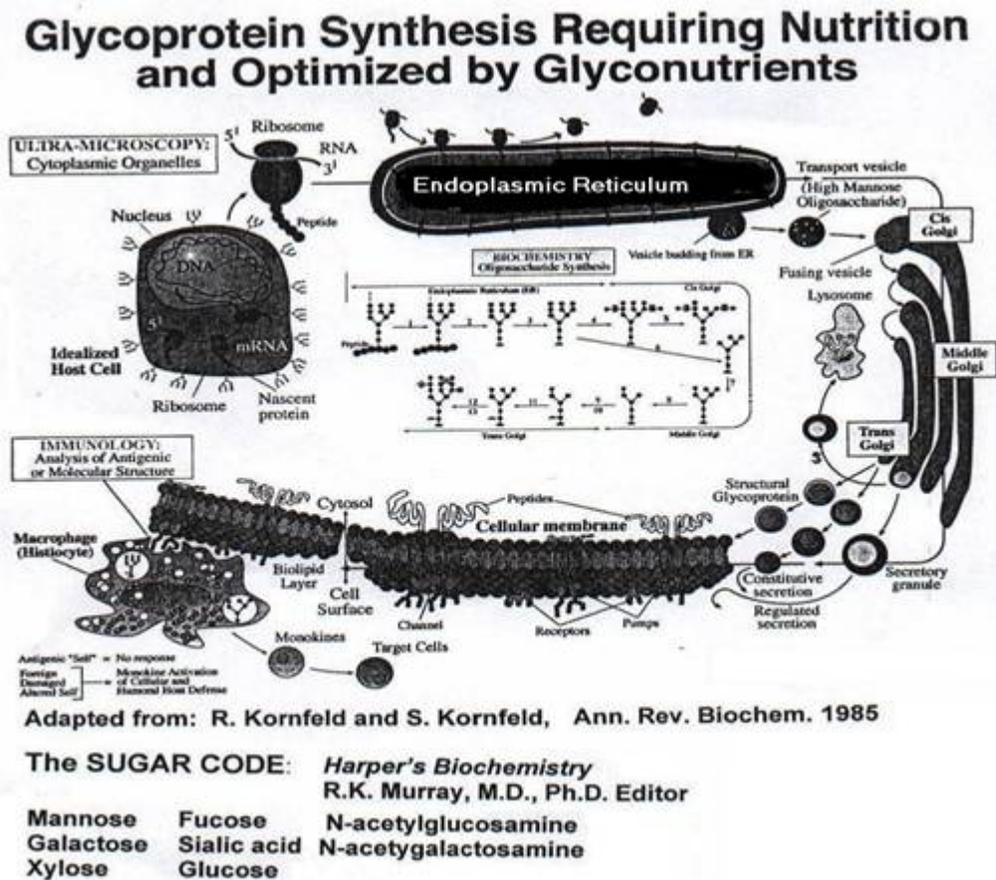
It is necessary to make an emphasis again that supplying the glyconutrient mannose is not treatment of a disease. Cancer cells or tissue culture lines that have been passed through cultures for many generations began to lose their ability to proliferate and will eventually die if not implanted in an animal and harvested anew. Adding mannose to malignant cells allows them to be revitalized and to grow better by the improved nutrition. In turn, the cancer cells may be implanted in a test animal and the abnormal cells will kill the creature. However, if the animal is given the concentrated glyconutrient it takes the same sugar molecules and makes anti-cancer cytokines at high levels that can be shown to attack and destroy the malignant cells. The body's cells use the nutrient to assemble natural, bioactive compounds under instructions coded in the genes to marshal innate or natural substances that protect the host. When put in the diet initially the glyconutrient has no capacity to attack and destroy the threat to life until it is incorporated into the structure of a previously non-existent complex molecular compounds that have bioactivity against abnormal cells. Nutrition is thus not the treatment of disease.

The body manages its own quest for defense, healing, balance and harmony between cells and physiological systems supported by ingredients in the diet. This is a totally different mechanism of action as compared to the mechanism of administering a direct acting pharmaceutical drug. Nutrition supports the engineering and design of life as written in the genome. Drugs interfere directly with the biochemistry and physiology of life and that is the basis for their toxicity that has led to the use of the "Black Box" warning for the impact of a poison and untoward side-effects of the more toxic drugs. .

The bio-assembly line present in each living cell is described in detail in the Kornfeld review that is contained in each human cell is graphically displayed in Graph I. This paper as it relates to our research efforts is metaphorically referred to as the Rosetta Stone for Cell Biology. This is due to its lucid description of the biochemistry and ultra-structure that provide a conceptual matrix for why nutrition is so vital in maintaining health, preventing disease, and restoring health. This is a paraphrase adapted from the DSHEA preamble that is the law of the land. This is the scientific foundation for the validity of the DSHEA legislation and Dr. Roger William's research theme. The Kornfeld paper emphasizes the role of sugars in glycoprotein synthesis. **However, this assembly line within every cell in the human body is a model for how elements from the periodic table numbering in excess of 70 and other nutrients such as amino acids, fats, sugars and vitamins are used as "parts" used to assemble structure/function compounds and provide catalytic activity that support the assembly line present in each living cells in the human body.** It must not be overlooked that the molecular structure of a compound determines its function. A more robust supply of nutrient and element units or parts for the assembly line in the cell optimizes the health and state of wellness for an individual.

An important fact is that in the bioassembly line (demonstrated in the center of Graph I) sugars are not only metabolized to provide energy as is the common limit of knowledge for the role of carbohydrates, but there is glycosylation (addition of sugars to peptides-amino acid chains and lipid or fat chains) in the endoplasmic reticulum and the Golgi. The significance of the coding capacity of sugars in glycoproteins and glycolipids is provided in a series of review articles in a glycoscience dedicated issue of Acta Anatomica.¹³ The addition of nine mannose sugars in three chain in the ER constitutes establishment of a domain on which instructions for life processes are transmitted between cells. In the Golgi other sugars are added and the number of mannose units are modified to provide a sugar code of information for conducting host defense, repair, growth, healing and homeostasis. This domain is the principle site for coordinating activities for the trillions of cells that make up the integrated community of cells in the human body. That is why supplying mannose from aloe gel resulted in the broad spectrum of health supporting benefits that constituted a disruptive technology for science and medicine.

Graph I



Caption Graph I:

The perimeter structures start with the model of an idealized cell. The central nucleus contains the chromosomes composed of chains of DNA that provide the code for cellular synthesis to conduct life processes. In the graph center is the progressive biochemistry that is conducted along the bio-assembly line to synthesize the final structure and function molecules shown at the bottom. A complementary working copy of the inherited DNA code for life is made called RNA. The RNA is audited for correct assembly (micronutrients are required for operating this step), and methylated if there are no errors and allowed to pass through the nuclear membrane into the cytoplasm. In the cytoplasm the three major steps of bio-assembly take place in the organelles called the (1) ribosomes, followed by the (2) endoplasmic reticulum (ER) (3) and Golgi. The peripheral cartoons are enlarged to show the idealized cell at app. 500 magnification and organelle details at app. 100,000 magnification. Amino acids are polymerized in the ribosome as the mRNA is drawn through the organelle and read much like a player piano roll to start the

symphony of life by forming peptides and protein chains. The peptide chain is taken to the ER and glycosylation (addition of sugars) starts by adding 9 molecules of mannose-6-PO₄ organized in three chains. This three chain domain is the basis for coding bio-information that is conveyed to cell membrane receptors. The mannose-rich glycoform is then taken to the Golgi for final assembly and code modification that includes substituting over 7 additional sugars for positions where mannoses had been initially connected.¹⁴ Glycosylation in the Golgi includes coding for a timer and address to determine how long the complex molecule lasts and where in the body the moiety is to be sent. The complex sugar code on the three chains convey charge and stereometric confirmation and constitute a means to communicate with other cells by fitting into receptor sites on cellular membranes. The component parts of the cellular membranes, including the receptor sites where cytokines interact, are also made on this assembly line.

In due time the passage of DSHEA brought the slow realization to our research group trained in the human sphere of physiology, pathology and medicine that defense, repair, regulation of cells, and healing is dependent upon and supported by nutrition. This was a slow developing and difficult step due to past education and training bias. Fortunately, this was not a problem for our team's veterinarians that shared with the human based professionals their profession's recognition of these facts known and used for generations. The bio-activity of the white powder from the aloe plant is in harmony with and supports normal physiology and in no way relates to the manner in which drugs function to relieve symptoms. Drugs substitute for or alter a bio-active molecule, inhibit an enzyme and act to block or alter normal physiology. This aloe-based micronutrient supports normal biochemistry that could potentially correct the basic problem causing the symptoms of disrupted normal physiology. This concept has been taught in veterinary schools for decades, but has yet to be widely recognized and taught in human medicine.

With this expanded viewpoint, the importance of supplying all the amino acids for the first step in bio-assembly in the ribosome and completion of glycoprotein and glycolipid synthesis in the Golgi was recognized in the past and is now expanded. It was realized that mannose and other dietary sugars are required in the Golgi to complete the proper assembly of structure/function molecules. The importance of fatty acids and related nutrients that are required to be able to properly synthesize lipoproteins cannot be ignored. To emphasize how intricate functional and nutritional requirements in cellular synthesis are, in the Golgi not only is the core structure completed, but each glycoform receives a coded address for its destination and a timer for how long the complex glycoprotein/glycolipid molecule is to exist. When the timer expires the ubiquitin system is activated via the lysosomal enzymes to initiate programmed cell death (apoptosis). Under ideal conditions this is accompanied by re-synthesis and replacement of the degraded structure/function glycoform that is initiated in the chromosomes by gene activation for replacement synthesis along the bio-assembly line described by the Kornfeld review. A wide array of micronutrients and elements is required to accomplish all these normal tasks of life because each step is carried out by a cascade of bio-active molecules synthesized in each cell. Optimal nutrition improves these biochemical processes.

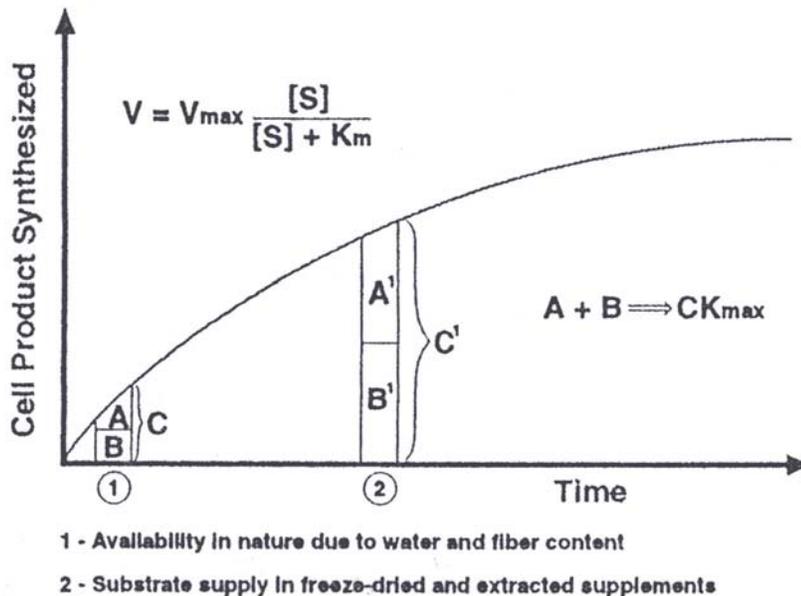
The plant kingdom was turned to and sources for other necessary dietary sugars missing in the modern diet were added to the polymannose of the aloe gel origin. When a more complete dietary supply of sugars was consumed as a daily supplement, all the desirable benefits of the mannose from aloe provided alone were found to be quicker, more complete, and the enhanced supply of more types of sugars was effective in supporting innate normalization mechanisms in more advanced disease states. Therefore, the body could heal and regulate itself more efficiently. This formulation was christened Ambrotose (Greek- Food from heaven or from the

Gods). In asthma and AIDS patients the bio-activity of the more complete supply of glyconutrients in Ambrotose and formulations to supply other micronutrients is estimated to be 5 to 20 times more than adding mannose alone to the diet (HR McDaniel 1989).

There is a principle of biochemistry that must be understood to be able to grasp the all too often inadequacy of the widely accepted dictum, “All one requires nutritionally for good health is a good general diet with variety.” One will also be able to see the value of supplying concentrated micronutrients and why such a step is a means to marshal a principle of molecular biology to generate biochemical power for restoring optimal health. The Michaelis-Menten equation and the curve it describes follows: ¹⁴

Graph II

Michaelis-Menten Biochemical Dynamics



Caption
Graph II:

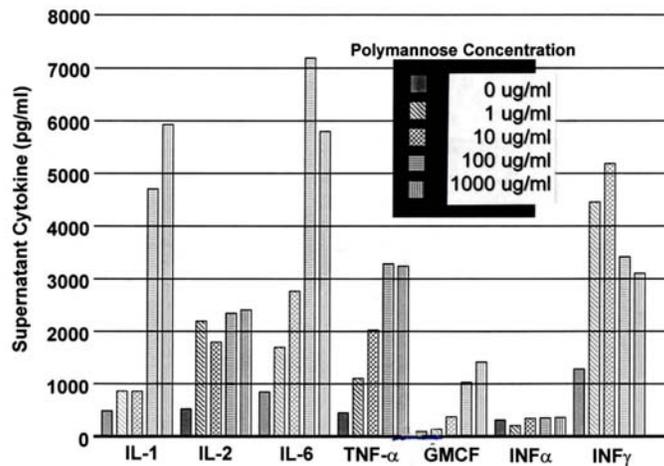
The graphic display is a description of the fact that within cells, if cell substrates are supplied, as in nutrient A that is combined with nutrient B to synthesize compound C, the more A and B that is progressively supplied, the more rapidly and greater is the amount of C that can be synthesized. It is essential to look at conditions (1) at the left where small amounts of C are synthesized. This is the status of foods as found in nature. For example, aloe leaf gel is 98.5% water. Fresh fruits and vegetables are over 90% water. A human cannot consume the volume of food to raise the cellular synthesis rate to the maximal production level shown at the top of the curve. However, by freeze-drying, as indicated by (2), through the removal of water one can place as a dry powder in a spoon, capsule or tablet, held easily in the hand several times a day, and consume the amount it would take weeks to consume as A and B occur in nature. In this manner, defense and healing mechanisms that serve to bring influenza or a common cold to an end naturally, can be taken to a new level of activity that can suppress HIV-1, hepatitis C viruses and other infectious agents. Thus, the power of innate mechanisms of defense and repair coded in the genes can be boosted to be effective against infectious agents and compromises in health that no medication has ever been effective. This is accomplished with virtually no toxicity and at a cost that is a fraction of pharmaceuticals that have a protective active patent.

To demonstrate the application of the Michaelis-Menten dynamics in dietary supplementation, the principle should and has been tested in cell systems designed to display the impact of increasing the nutrient supply of glyconutrients to cells involved in synthesis of defensive and

reparative cytokines (see Graph III). One should note how closely several cytokines of the inflammatory cascade conform to the dynamics predicted by the Michaelis-Menton curve. Only synthesis of interferon alpha is not increased by increasing the supply of aloe polymannose in the mixed-leukocyte cultures.

Graph III

Cytokines Produced by Human PBMC After Culture with Polymannose Glyconutrient



G. Marshall, et al., *Amer. Acad. Aller. Immuno.*, 1992

Caption Graph III:

The series of bar graphs display the average for three or more leukocyte cultures to which standard medium has been used as the control and then three progressive increase in concentrations of aloe polymannose has been added to the cultures ¹⁵. The control ELISA assays are at the far left of each cytokine assayed. Note that there is a general increase in cytokine production as each increment of the glyconutrient is increased, except for interferon alpha. Clinical results in human subjects with health compromises follow the same general response trend.

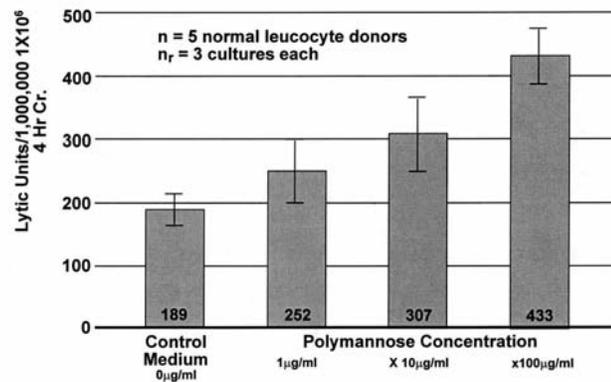
The informed critic might now state, “This *in vitro* study ¹⁵ indicates that there is an increase in the production of cell to cell communication molecules that would be active in up-regulating the general defense of the body. How do you know that these cytokines are functional and carry out instructions to destroy an infectious agent or abnormal cells?” In 1993 the first of a series of experiments to demonstrate whether effector leukocytes receive and respond to the increase release of cytokines and are recruited into a defensive activity. ¹⁶ Graph IV demonstrates the summation of this work. A tissue culture cell line is seeded with a herpes virus that the cells will take into their cytoplasm. Chromium-51 is added to the medium and it is taken into the virus-seeded cells. All excess virus and radioactive isotope is washed out of the culture. The virus and radioactive isotope are now only present within the living cells contained within intact cellular membranes. Leukocytes are incubated in the same manner as in Graph III, then harvested after a 24- hour growth period in an increasing concentration of aloe polymannose-enriched medium. These mixed leukocytes contain activated natural killer lymphocytes (NK). The mixed leukocytes are added to the target cultures of previously prepared virus and isotope-

loaded target cells. It is a normal act of defensive physiology for NK cells to detect virus-laden cells and to destroy them, so as to prevent further synthesis of virus particles. This is done by the NK cells releasing perforin, an enzyme that cuts holes in the virus infected cell's cellular membrane to destroy it. If the NK cells are activated to attack and destroy virus infected cells by cytokine transmitted instructions, and if the amount of cytokines synthesized influences the rate at which holes are cut in the virus laden cells, then the release into the medium of the radioisotope will be proportional to the amount of aloe polymannose supplied in the initial leukocyte cultures. Note that Graph IV demonstrates that the release of Cr-51 into the target culture cell medium, evidence for destruction of virus infected cell, and the level of isotope follows the amount of mannose supplied to the leukocytes in Graph III that demonstrates enhanced step-wise synthesis of defensive cytokines.

Graph IV

***In Vitro* Effect of Polymannose on Human PBL in 4 Hour NK Cytotoxic Functional Assay**

Destruction of virus Cells



loaded

G. Marshall, J.P. Drack, *Clin. Immun. Society*, Abstract 1381, May, 1993

Graph IV relates to cells in tissue culture that were seeded with herpes virus, chromium-51 isotope was added to the chambers and all material not intracellular was washed-out. Leukocytes from peripheral blood were pre-cultured with an increasing amount of aloe polymannose in a complete medium. The leukocytes were then added to the virus laden target cultures. Note that the release of intracellular chromium-51 (the height of the bars) is proportional to the amount of aloe polymannose supplied to the leukocytes. This is an assay designed to show the influence of the amount of glyconutrient supplied on the production of cytokines and resulting antiviral activity of NK cells. This is a demonstration of the innate antiviral mechanism that is operational when human beings recover from influenza or a common cold without medical intervention.

The confirmed cynic or cautious observer will undoubtedly respond that this series of experiments are all in cell cultures and the results cannot be transferred to inferences about what might be expected to happen in an animal or man. These *in vitro* experiments in no way include or contain the complex interactions of multiple defense mechanisms that are active in the human

body or *in vivo* in an intact animal. That is correct. If an antiviral study was conducted in human beings, an expensive and ethically challenging project, there would be multiple confounding variables ranging from genetic make-up to dietary variations. However, 20 cats divided into 10 controls and 10 intervention subjects, on the same diet were challenged with a feline rhinotracheitis virus nasal wash.¹⁷ The test animals had a dietary loading with aloe polymannose 15 mg/KG administered 6 hours before the viral challenge while the controls were given sterile saline nasally. There was a 100% infection rate in the controls with all animals having symptoms for over 30 days. One control died of pneumonia. In the intervention group that received a single aloe polymannose prior to the exposure, 8 animals had no symptoms what so ever. Two had red eyes and nasal discharge for two days and were free of symptoms.

At this point it is a reasonable question to ask why, as follows in the following pilot studies, the status of such different health problems in human subjects can be improved by the addition of micronutrients to the diet? And why don't all health providers know and use this simple, effective, and economical nutritional technology? More specifically, how can the same micronutrients being represented as active in preventing or arresting infections, improving body composition, percent fat, percent muscle, and increase bone density, be related in any manner to behavior and learning problems of children with attention deficit disorder (ADD)?

To do the research in order to supply the detailed answers modern science demands will require millions of dollars. The publication of pilot studies is to provide information that may assist in initiating an interest and the granting of funds to support inquiry into this approach for managing or eliminating health compromises. The status of micronutrients is not one for being recommended as a national policy or professional recommendations. Further study is judged to be warranted. Unfortunately, a block to this has been found to be attitudinal in nature. It is not a unique trait of scientists to reject and seriously question new ideas or methods to address old unanswered problems that are also financially rewarding sources of professional activity. It is a human characteristic to hold something newly discovered or recognized as suspicious, if not a candidate to be shunned or rejected. If a potential solution would limit future profits in a sickness industry, there are other incentives to oppose a new modality that has a hint of potential success. The intent of this research team is to trudge forward on the demanding road of evidence based-medicine. The end of this journey is recognized to be beyond the horizon, far in the distance traversing a mine field created by scientific and medical self-interest preserving opposition.

The reaction to a different idea or new method can be complicated. If, for example, micronutrients were to be added to the diet for millions of school children and grades and department significantly improved, it just might be responded to as an indictment of those who have spent billions in public funds unsuccessfully trying to correct such a serious national problem. The school system of California is in the process of spending 5 billion dollars on this educational problem. Thus far, no statistically significant progress can be detected.¹⁸ There are those in positions regarded as experts and authorities in positions of power, respect, and responsibility with reputations built on other approaches to solving the problem in the schools. Teaching and training programs at universities offer special programs providing qualifications and specialties that would destroy professional empires if micronutrition solved this problem in public education. Thus, what appears to be a simple correction of a public problem attacks an

industry based on the problem not being solved and certainly not by something as simple as giving micronutrients. This scenario also applies to leaders and those of prominence in science and medicine regarding other unsolved compromises in health. The following pilot studies provide suggestions for further study that only scratch the surface for multiple observations for improved health benefits associated with better nutrition. Those in scientific and medical research and teaching who for decades in the past, and anticipate in the future, receiving public and private sources for funding decades of research could be less than thrilled to find that micronutrients seriously alter or eliminate their future career plans. This closes the experiences with the attitudes and actions of peer investigators who might be threatened by this nutritional technology that puts the power to manage health in the hands of patients or lay families.

One should know that dozens, if not hundreds of anecdotal reports from a wide geographic range, including multiple countries and ethnic groups, are received about improvements seen in a diagnostic entity or study focus, before a pilot study is organized. The results for problems reported are quite narrow and small compared to the total experience of the last 23 years of seeing and hearing of patient responses directly or from their physician.

If the following simple summary is not the mechanism of action for all the observations reported in this monograph, then this correspondent is clueless to the cause and effect for the wide range of benefits that are being reported and even a wider spectrum of favorable responses that have been observed in many persons.

Each of the trillions of cells in the human body contain the bio-assembly line described in more detail above. This bio-assembly line requires thousands of nutrient molecules and elements to be able to assemble the compounds that make up the structure and function of the body. Instructions for the synthesis conducted on the bio-assembly line are inherited from our parents and stored as coded instructions in chains of DNA in the center of each young cell. (Skin cells and erythrocytes are examples of cells that lose the nuclear DNA and bio-assembly line as they mature.) The biochemical processes we observe as life require the synthesis of complex molecules to form the structures of the human body and operate the cells, tissues, and organs. Nutrition to supply all molecules required for cellular synthesis is absolutely vital for normal function and to restore proper operation of the body. The fundamental relationship and interdependency for nutrients to support biochemical synthesis and function for all cells is paramount to each and every cell. A complete supply of nutrients is vital to restore physiological balance and communication within the body for a distended adipose tissue cell loaded with fatty substances that need to be mobilized and utilized for energy through action of the pituitary, thyroid, adrenals and mitochondria. A network of neurons in the brain of a youth require optimization of nutrients to be able to learn facts, operate the mechanisms of recall, process cognition, relate such knowledge to needs for performing on tests or living, sometimes surviving each day. It is an almost revolutionary premise to exclaim that in the functions of the human body conducted ultimately at the cellular level, and recovery from disease orchestrated at the cellular level, that the supply of all nutrients optimizes the function of all cells under normal conditions or efforts to restore normalcy. This nutritional requirement includes not only the nutrition to support the act of running from a life threatening danger or sprinting to receive a reward, but the thinking, cognitive processes that determine the direction that is appropriate for the individual to choose and then follow to survive or be honored.

It has taken the reader only a few minutes to follow the narrative provided in an attempt to share experiences that have taken over two decades for the author to travel. Few could have been more skeptical when first informed in 1985 that AIDS patients were reporting significant benefits from drinking a specially stabilized aloe beverage. The slow addition of other micronutrients to the diet that are low or missing in the modern urban food chain has been found to far exceed what has been provided in the cases that are mentioned in this manuscript. It is hoped that this information will drive the reader to test the assertions and representation that have been made.

A final testament to the simplicity of this nutritional technology is the fact that these principles are not based on new dynamics that have recently begun to occur within living cells. The health benefits that follow in the papers provided relate to recently recognized phenomena of life that are as old as living cells, that is, life itself. The intricate design and engineering of the bio-assembly line present in each and every young living cell is awesome to contemplate. However, consider now that in natural food, whole foods, that the micronutrients that have been identified in recent years are required for proper biochemistry. These nutrient molecules provided in the environment of earth have a profound impact on optimizing the health of human beings and are naturally present in plants. There seems to be an intelligent provision integrated with the biochemical engineering requirements of cells to conduct life on this planet that simply is a supply of nutrients that cells require for good health, to prevent disease, and restore health, as is stated in the preamble of the DSHEA. Certain necessary nutrients for proper cellular synthesis, the glyconutrients and fatty acids, can be uniquely found in human mother's breast milk¹⁹ not in cow's milk or other mammal's milk. The exquisite and detailed requirements for optimal biochemistry conducted in the cells is not only provided for in mother's milk during dependent infancy, but is then present in nature for the adult as described in Genesis 1-29. Amid the oldest coherent human writing that is available in the scrolls of the Torah we find stated, "And I give you the herbs and seed bearing plants, for you it shall be meat," (KJ, 1611 translation). Hebrew scholars state that the translation to English is good poetic imagery and accurate, but a more literal statement would be, "...for you it shall be sustenance."

The growing evidence is that this simple phrase echoing wisdom across the ages is not only poetic, but factual and of an immense value to humankind.

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