Cancer can be Prevented!

Inositol + Cal Mag IP_6

"The scientific merits of this important natural product are expressed with clarity and understanding. Though considered by many as nature's premier cancer fighting supplement, Dr. Vanderlinden explains how everyone can benefit by using what has been hailed as the "Natural Product of the Decade."
Dr. Michael T. Murray, N.D.

Cancer will be our #1 Killer!

In April 2004 the Canadian Cancer Society released a report indicating that in the next two decades cancer would surpass heart disease as the #1 killer of Canadians.

"I understand as individuals that most of us don't like to even think of cancer if we don't have to, however... I think it's simply a case of not realizing there's something we can do."
Dr. Kim Vanderlinden

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TOO GOOD TO BE TRUE? Dr. Kim Vanderlinden N.D., D.T.C.M. Dr. Ivana Vucenik Ph.D.

Inositol + Cal Mag IP_6

TOO GOOD TO BE TRUE?

Prevention & Treatment of:
Cancer,
Osteoporosis,
Depression, Diabetes,
Heart Disease & more...

Dr. Kim Vanderlinden N.D., D.T.C.M.
Dr. Ivana Vucenik Ph.D.

TOO GOOD TO BE TRUE?

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One of Nutrition's best kept secrets

This naturally occurring, yet potent antioxidant is now being researched around the globe for its value in the prevention and treatment of:

Cancer	**Osteoporosis**
Diabetes	**Heart Disease**
Depression	**Kidney Stones**

Dr. Kim Vanderlinden N.D., D.T.C.M.

Dr. Ivana Vucenik Ph.D.

I have always felt that medicine should be about sharing. About the sharing of information that can help us lead happier, healthier lives. I feel very privileged to be able to share this remarkable story with you.

Dr. Kim Vanderlinden

Forward 1

Three main reasons justify the attention of the medical community to the pharmacological effects of Inositol-6-phosphate (IP_6):

1. Experimental results produced and reported independently by many eminent researchers, working in more than 100 laboratories all over the world, have shown that IP_6 acts as a natural regulator of normal cell life 1,2 .
2. Furthermore, IP_6 has exhibited a remarkable capacity to control cancer cell growth both in vitro and in vivo. Adequate explanation of the mechanism of this action has also been presented 1,2.
3. Numerous testimonials of the beneficial preventive and/or therapeutic effects and the absence of any side effects of IP_6 exist. These effects concern cancer, cardiovascular disease, kidney stones, diabetes, osteoporosis and depression.

This book describes explicitly the current knowledge on IP_6 converting the solid scientific facts in to a promise for better human health.

Dr. John Delinassios Ph.D.

Director International Institute of Anticancer Research

Managing Editor of the Medical Journals:

Anticancer Research

In Vivo

Cancer Genomic and Proteomics

[1] Shamsuddin AKM: IP_6: Nature's Revolutionary Cancer Fighter. 1998, Kensington Books

[2] Anticancer Research Volume 19, No. 5A pp.3633-3791 Special issue on Disease Prevention by IP_6 and Other Rice Components, edited by T. Ishikawa, S. Ogawa and AKM Shamsuddin

Forward 2

It was a fortunate occasion when I met Professor Shamsuddin in London a few years ago. It was not only heart warming but also a very educational talk, and I was most interested in his subject “How to help Cancer Patients”.

Complementary there is a lot, which can be done to help with Cancer, and as I have often said in my lectures, “Cancer is like a warfare between two armies of cells, the degenerative and regenerative cells”. Very often with aggressive treatment both cells are killed.

Professor Shamsuddin has researched for many years how to control cancer cells, and how to support the regenerative cells in order to fight the degenerative cells.

When Professor Shamsuddin found the small ingredient in a rice grain that could possibly control cancer cells, this was a major breakthrough. After all cancer cells are really cells out of control.

This monstrous disease called “Cancer” requires a lot of attention. As a result of Professor Shamsuddin’s experience and my own, we both agree that through knowledge and advice on natural methods and natural medicine it is possible to improve one’s health and keep certain conditions under control.

Nature itself is capable of healing but it often needs some guidance and advice from experienced people, in another way prevention is better than cure. Today in a world where cancer is so much on the increase this principle plays a major role. The fact that we are born in nature, we belong to nature we have to learn to think a little bit more biologically. In this great scientific world, one has to be careful not to overlook these facts.

The second time that I met Professor Shamsuddin was from a different angle. We were fighting very, very, hard for the life of a dear friend. I found out then, that not only was he a very intelligent

researcher, but he was a man who had a real heart for people. These two things combined have made him a unique person.

Professor Shamsuddin has contributed to humanity through his tireless research efforts, which he has carried out with great compassion. Often facing political and economic hurdles, Dr. Shamsuddin has instinctively researched areas that contradicted the conventional dogma of the day. Dr. Vanderlinden has captured the essence of this struggle. Today Dr. Shamsuddin is not alone, as many top scientists have sought to explain the healing properties of IP_6.

The author, Dr. Kim Vanderlinden's family has been confronted with cancer a number of times. Highly motivated, his search for an effective, evidence based, cancer preventive ultimately resulted in him meeting Professor Dr. A.K.M. Shamsuddin. As you will read Dr. Vanderlinden was fascinated with the professor's work as it held true promise. Dr. Vanderlinden has captured the significance of this safe, natural, and most important preventive medicine and presents it in a format for all to benefit. This book provides exciting new research, and brings a ray of hope and light to the human suffering of this monstrous disease. It is written in a style that is understandable by all and at the same time has the substance and mechanisms of action that will appeal to physicians and those in the health care field. In addition to the cancer theme, Dr. Vanderlinden relays upon his clinical experience and questions current dogma in other areas such as depression or heart disease as well.

I am sure that the book will be valued by everyone who reads it, as Inositol + Cal Mag IP_6 is surely one of the safest and most important preventive medicines today.

Professor Jan de Vries
Auchenkyle
Southwood Road
Troon
Scotland.

TOO GOOD TO BE TRUE?

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Introduction

Returning from the 1998 Kyoto international medical conference on IP_6 and Rice Components, I turned to my colleague and stated that I'd never been so excited about a supplement! All the way from Japan back to Vancouver I could hardly contain myself, rambling on and on about the medical implications of this natural medicine. Here for the first time was a food based supplement with the power to prevent one of our most dreaded diseases; cancer. It wasn't as though I hadn't been excited about natural medicines in the past. For the previous 6 years, in addition to practicing I had been lecturing and helping with the initial introduction into Canada of several innovative, leading edge natural medicines such as glucosamine, black cohosh, DGL and St. John's Wort etc. However, because of a family history of cancer, I couldn't wait to spread the word of this simple, yet extraordinary, rice extract knowing cancer's devastating effects.

My only aunt died of breast cancer and my grandmother of leukemia. However, it was my mother's battle with Hodgkin's lymphoma that had the deepest impact. When I was 12, my mother was told she had advanced cancer and was expected to survive only a few months. Desperate, she was willing to try anything. Her journey landed her in a Naturopathic physician's office. Dr. Skaken had a Ph.D. in biochemistry and was keenly aware of the impact food has on health. In addition to her diagnosis of Hodgkin's, he suggested that her problems may have started years ago when delivering my sister. At the time she had lost a lot of blood and was fatigued ever since even though she was not anemic. He had her eat a pound of raw calf liver daily to rebuild her blood. The smell was so disgusting that each day we stayed outside while she tried to down the liver. However, after a few months she was transformed from a weak can-

cer stricken patient that was expected to expire into someone with an abundance of energy. In the case of cancer, the saying “an ounce of prevention is worth a pound of cure” is very understated, especially if raw liver happens to be the medicine of choice. At the same time she also sought help from a Native American Shaman that held traditional healing sweat lodges. After she returned from the sweat lodges the first time, her oncologist was confused as her cancer was regressing. Seven years later my mother had a relapse and landed in the hospital. Within a short time she was in a coma and again expected to pass on. At one point her doctor said she would not make it to the morning. That night my dad returned home from the hospital. He hadn’t spoken with the shaman in 2 years and decided to give him a call. Before he had a chance to speak and identify himself, the shaman’s wife answered the phone (this was decades before call display or caller ID) saying not to worry, as they had sent “Help” and that my mother would be fine by the morning. In shock my dad just dropped the phone. Miraculously, the next morning my mother came out of her coma and lived another 15 years Hodgkin’s free.

With my family history I was always on the lookout for preventive cancer strategies. Dr. AKM Shamsuddin has given us more, much more. Inositol + Cal Mag IP_6 is not only a major preventive, but a most valuable adjunctive therapy as well. He has also discovered early stage cancer screening tests. See www.imimedical.com Early detection dramatically increases the chance of survival when cancers are found prior to spreading. PREVENTION * TREATMENT * EARLY DETECTION. What contributions! Even a small advancement in any of these areas would be considered a significant lifetime achievement for many scientists.

How can it be that most persons and medical people are not familiar with his work? I believe that there are two underlying causes. First, his concepts are:

TOO SIMPLE

Cancer is normally considered very complicated, as it is not one disease, but several: lung, liver, colon, breast etc with several causes:

diet, smoking, genetics, radiation, bacteria, viruses etc. In fact only minimal variations exist between healthy and cancerous cells. They are far more alike than they are different. Almost all of our cells contain signalling molecules called phosphorylated inositols of which IP_6 is one. These molecules have several functions and one of them is a regulatory effect on the rate of cell division.

The lab tests developed by Dr. Shamsuddin in reality are also quite simple. They detect an abnormal sugar that is secreted only by precancerous or cancerous cells. His contributions are profound yet their simplicity may inhibit the acceptance by current “experts”. Experts who, in many cases, have invested their professional careers attempting to understand the differences between the various cancers. Secondly:

CHANGE IS DIFFICULT

A fundamental change in perspective is necessary if one is to even consider Inositol + Cal Mag IP_6 as a chemotherapeutic agent. Unlike other chemotherapeutic agents, it is not toxic and does not kill cancer cells. However, it does help control cancer cell proliferation or growth. In reality an agent that doesn’t harm healthy cells while inhibiting cancerous cells would be the ideal agent. The concept of a non-toxic chemotherapeutic agent maybe too radical an idea to grasp, since it challenges the very premise upon which chemotherapy has been based. Great scientists are naturally inquisitive, always seeking answers to explain their observations. The chapter on the National Cancer Institute highlights the difficulty of presenting fresh ideas, as some of the head scientists in the organization seem uninterested in explaining observations that do not comply with current models-models that seem intent on developing toxic molecules from which to wage the war on cancer.

In my private practice I have often witnessed a resistance or inability to change treatment strategies. The fundamental question for physicians is: WHY? Why did the patient get better? Or, why didn’t the patient get better? Perhaps the best example I can think of is the management of stomach acid levels, which involves the treatment of heartburn, acid reflux, hiatal hernia and gastric/duodenal ulcers. Prior to Inositol + Cal Mag IP_6, my favorite lecture topic and natural

medicine was DGL (short for deglycyrrhizinated licorice). DGL is very effective at enhancing the production of the protective mucin coating that lines the digestive tract, which enables us to resist the corrosive properties of the digestive acids. In addition, DGL has a mild inhibitory effect on H. Pylori, which are bacteria that are also known to cause heartburn. One case stands out in my mind from years ago. The patient had two operations, each time removing a heavily ulcerated portion of her stomach. She was in constant pain and as a result was scheduled for a further surgery in which the vagus nerve to her stomach was to be severed [the vagus nerve is necessary for acid secretion]. The side effect of this operation is often uncontrollable diarrhea, as the vagus nerve also serves the intestines. DGL corrected her problem quickly and no operation was necessary. I never received a call from her doctor, specialist or surgeon. Wouldn't you think that as physicians that they must have been at least a little curious as to why the sudden change in their patient's long standing condition occurred? It's my guess that these physicians did not change and continued to treat heartburn/ulcers in the same manner even though they had a patient sitting right in front of them that held the answer to a better way.

I have the deepest level of respect for Dr. Shamsuddin as a scientist. He sought an explanation for inconsistencies in cancer data derived from various study populations. The conventional wisdom and dogma of the time suggested that it was the quantity of fiber consumed that reduced colon cancer risk. In other words, the more fiber you ate, the less risk you had of developing colon cancer. He didn't overlook the inconsistencies from population studies, but instead performed experiments searching for a reason as to the discrepancy. As you will see, this curiosity has led to nearly two decades of research. In addition to cancer prevention and treatment, research on the IP_6 molecule now shows promise in other important areas as well such as: osteoporosis, cardiovascular disease, mood disorders, immune system support, kidney stones, diabetes and anti-aging medicine. His research has sparked international intrigue resulting in further investigation at laboratories around the world. Dr. Shamsuddin's research efforts have provided answers and raised further questions with profound medical and societal implications for all of us and for which I am most grateful.

The Chicken or the Egg?

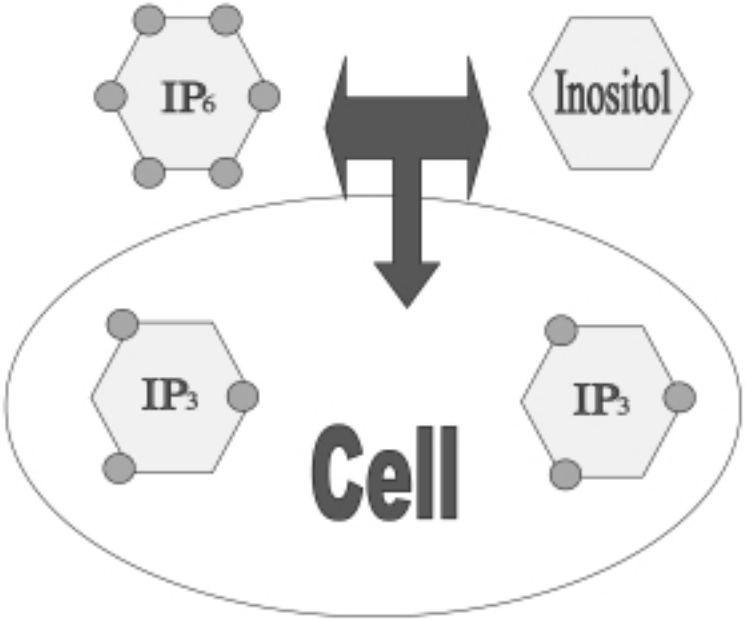
Which came first, inositol or IP_6? It's tough to say as the body makes inositol out of IP_6 by removing the phosphate groups and conversely, makes IP_6 from inositol by adding phosphate groups. There are several overlapping and complementary effects on our body resulting from these two molecules. This question becomes even harder to answer when one realizes that the body produces some of its own and at the same time also relies on a dietary source of both molecules for optimal health.

There are a number of very important instances when the two molecules have been proven to augment each other, resulting in a stronger, more pronounced effect.

Communication within a cell, between the various organelles and molecules is called cell signaling. An important cellular messenger effecting cell signaling is called IP_3 or inositol triphosphate. IP_3 is made up of inositol plus three phosphate groups and is therefore at the midway point between inositol and IP_6.

IP_3 levels have a distinct effect on the rate of cell division. This has major implications when it comes to cancer. If the rate of cell division can be slowed down or made to normalize, then the impact of cancer on the body can be much less. A transient increase in the level of IP_3 results in a signal for cell division; indeed, increased levels of IP_3 have been found in various cancer cells. Based on the observation that populations who eat an IP_6-rich diet enjoy a low incidence of cancer, Dr. Shamsuddin found this to be paradoxical. Paradoxical because, within the cell increased IP_3 results in cell division, yet on a population basis people who ingest more IP_6 have

less cancer! Combining the two conflicting observations, he hypothesized that a **nutritionally sufficient** [increased] level of intracellular IP_3 should normalize the rate of cell division as that's what happens to people who consume a healthy diet. As you may note this hardly makes any sense; he too realized it and thus did not spend any time discussing with his colleagues lest he drew ridicule that he received anyway! Instead, he went to the lab and did the experiments to prove or disprove his hypothesis to himself. By giving IP_6 to cancer cells, he could increase the level of intracellular IP_3 that paradoxically resulted in a decrease in cell division! Experiments showed that to be true across species and cancers. He then added IP_6 to inositol to increase the levels of IP_3 even more. And the results were consistent, the combined treatment of Inositol + IP_6 was clearly better than inositol or IP_6 on their own.



1.1

You will read the term "Inositol + Cal Mag IP_6" throughout this book. The "Cal Mag" portion of the formula name simply refers to the calcium and magnesium to which the IP_6 is bound. Other minerals such as iron or sodium can be bound to IP_6, in which case you would have iron IP_6 or sodium IP_6. In the majority of people, having additional calcium and magnesium would offer the most health benefit, especially with the alarming rate of osteoporosis.

So which came first? I don't really know, however since inositol is commonly referred to as "The Mother of IP_6", we will start by exploring inositol.

Inositol

In addition to highlighting the many health benefits of this rice bran extract, the reason I am writing this book, is that I believe Inositol + Cal Mag IP6 is our most important means (besides a healthy lifestyle) by which to prevent cancer. I first learned just how important the supplement was at the IP6 conference in Kyoto Japan in 1998. While attending the conference I was fortunate to hear Dr. Lee Wattenberg speak. I will never forget the title by which he was referred: “The Father of Chemoprevention”. What a career and what contributions this professor must have made.

As I understand professor Wattenberg’s history, for several decades he searched for naturally occurring compounds that could theoretically prevent cancer and then applied scientific methodologies to research them. After testing several molecules, he found inositol to have great potential. Then using various study models he was able to demonstrate that inositol could prevent lung cancer. As lung cancer is by far the most deadly cancer in terms of the total number of deaths, this was a major finding. Previously we knew that a poor diet could increase cancer incidence, but now Dr. Wattenberg’s research showed that a common nutrient could actually prevent cancer. A truly empowering discovery, implying people could use a nutritional supplement to lessen lung cancer risk.

I’m actually surprised that cigarette companies aren’t somehow taking advantage of this professor’s research. Perhaps they are and I just haven’t heard of it. As inositol is inexpensive, I’m sure that cigarette companies could consider handing out a bottle of inositol with a carton of cigarettes---what do you think? Of course that would be

admitting that cigarettes cause cancer, but I believe that the "secret" may have already slipped out.

Very early on Dr. Shamsuddin also showed that inositol was able to prevent cancer. In his case he was able to demonstrate the preventive value of inositol with colon cancer. Besides cancer prevention, inositol affects our health in several ways, largely because it is in all of our cells and in addition, is a major component of our cell linings or membranes. The brain, sperm, testicles and epididymis are believed to contain the highest levels of inositol.

Throughout the book you will find more detailed descriptions of inositol's health benefits. In addition to cancer the conditions which may benefit from inositol supplementation are listed below to provide a quick preview.

1-diabetic neuropathy
2-diabetic birth defects
3-neural tube defects
4-fatty liver
5-depression
6-panic disorder
7-obsessive-compulsive disorder
8-brain seizures
9-cholesterol levels
10-triglyceride levels
11-antioxidant for premature aging

Being a natural compound, there is little incentive for drug companies to research inositol. Despite a lack of financial reward, you can still see how many researchers are studying the effects of inositol, by using www.pubmed.com. The number of the studies appearing on Pubmed are listed at the beginning of the reference section, which you will find at the back of this book.

Unlike IP_6, there are also substantial animal sources of inositol. If you recall, in overcoming her Hodgkins lymphoma, my mother consumed massive amounts of calf liver. Perhaps the inositol she would have been receiving played a role.

Food Sources of Inositol

Beans, dried	Nuts
Calves' liver	Oats
Cantaloupe	Pork
Citrus fruit, but not lemons	Rice
Garbanzo beans	Veal
Lecithin	Wheat germ
Lentils	Whole grains

Inositol is considered as part of the B complex group of vitamins, even though it's not officially recognized as a B vitamin and no RDA has been set. Clinically, one can see an overlap with the B vitamins as well, since B vitamins are used for several of the conditions listed above. Inositol like the B vitamins is water soluble (it mixes with water) and as a result is not stored very well in the body. Therefore, inositol has to be continually replaced dietarily, even though approximately 4 grams a day are produced from glucose by the kidneys.

In the laboratory when growing human or animal cells, it's necessary to add inositol to the growth media, for without it the cells cease to grow. It's easy to see why inositol is considered an essential growth factor. As it is considered to pose no health risks and is considered essential, inositol is normally added to infant formulas, which further illustrates its importance nutritionally.

Fiber: Friend or Foe?

For the last three decades scientists have generally considered fiber to be the protector of the colon. Investigations of various populations determined that the higher the fiber consumption the lower the incidence of colon cancer. However, when the people of Finland and Denmark were compared, the results were confounding. Here for the first time was evidence that greatly conflicted the previous research. The Danes on average consumed more fiber, yet had twice as much colon cancer as compared to the Finns. If the fiber theory was correct, then the colon cancer incidence should have been less, not more as in Denmark. This is where this amazing story begins!

As Dr. Shamsuddin tells it, in the summer of 1985 he was looking through the medical journal “Cancer”. As a MD and pathologist he specialized in colon cancer and was intrigued by an article by Drs. Ernest Graf and John Eaton of the Pillsbury Company called “Dietary Suppression of Colonic Cancer: Fiber or Phytate?” In the article the authors questioned whether fiber consumption did in fact prevent colon cancer. The Finnish people ate most of their fiber in the form of cereal, which is high in phytate or what is now known as IP_6. What was protecting the Finns? Was it the IP_6? It was anybody’s guess. No one really knew.

What if Graf and Eaton were correct? The implications would be enormous. Colon cancer is the second deadliest cancer in America. Were the current dietary recommendations wrong? Was an extremely important nutrient being overlooked? As you will read, what follows next is nearly two decades of research. A journey that forced Dr. Shamsuddin to go against the flow by questioning the conventional wisdom of the day. In his quest for answers he was subtly

ridiculed by some and even called a failure by his department head, as his research wasn't considered important enough to attract research grants. All this because he wanted to know the truth. To make matters worse, phytate or IP_6 had been identified over a hundred years ago (1855) and was generally considered to have a negative impact on nutrition, as it was believed to hinder mineral absorption. Would the bad guy phytate turn out to be the good guy IP_6?

Before we investigate the controversy it would help to have a basic understanding of what fiber is.

Most of us are generally correct in thinking of fiber as the indigestible portion of the plants we consume. Fiber is formally divided into two main groups. Soluble fiber, which can be partially digested by the enzymes produced by our intestinal flora. Soluble fiber generally doesn't absorb as much water and therefore won't bulk up the stool as well. Soluble fiber is found in fruits, vegetables and some grains such as oats. Insoluble fiber is more resistant to the digestive process and as a result is a better stool bulking agent. Grains are the major source of insoluble fiber. The highest concentration of fiber is most often in the outer coating or bran portion of the grain.

Fiber has experienced periods of both popularity and anonymity over the years. More recently fat has been in the limelight, as high fat diets have been linked to various conditions including cancer. In some cases the facts seem clear: i.e. eat more fat and a woman's risk of breast cancer goes up. Fat has become for many public enemy number one. However, are we listening to mere facts and missing the big picture? Are we jumping to conclusions too quickly? Are we in fact missing out on the truth? Ponder this: Consuming fat is generally more satiating and will naturally lead to fewer carbohydrates and therefore less fiber being eaten. Are many of our health problems due to too much fat or due to the resulting decrease in fiber containing carbohydrates?

I don't know the answer. I would however expect that if one were to suggest that over consumption of fat was not the culprit, that very likely they would receive the same "warm" reaction that Dr. Shamsuddin did over the years by suggesting that fiber consumption may not be protecting us to the degree commonly thought. Dare we speak against our protectors (fiber) and for our enemies (fat). As you can well imagine, obtaining research grants and institutional support (i.e. The National Cancer Institute) was always an uphill battle for him.

What's in a Name?

By now you realize that much of this story centers around phytate or IP6, which are just two names for the same molecule. Phytate is the more traditional name with IP6 gaining popularity in the last decade. You may also hear the molecule referred to as Cal Mag IP6, sodium IP6, iron IP6, phytic acid, inositol hexaphosphate or inositol 6phosphate.

To add a little confusion there are actually a number of different types of IP6. The molecule exists on its own [inositol hexaphosphoric acid] or can be bound to various minerals such as calcium, magnesium, iron or sodium [in nature as Cal Mag inositol hexaphosphate] . The type that contains what I believe are the most beneficial minerals is called Cal Mag IP6, as it is complexed with six molecules of calcium and magnesium; how interesting that it occurs naturally in its most beneficial form!

Is phytate or IP6 a type of fiber? No, it exists in both plant and animal cells, but the confusion arises because the highest concentrations are found in fiber, especially insoluble fiber. In fact IP6 is found in many places, including the soil and in all of our own cells. To get levels high enough to influence our health we rely on plant sources. Corn happens to have the highest levels, however as a supplement, IP6 is often extracted from the bran of rice, which is removed when brown rice is polished and converted into white rice. Common food sources of IP6 can be found in the inset pictures on the next page.

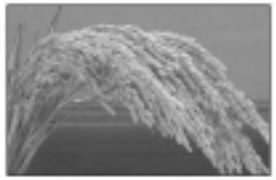
4.1

IP_6 Contents in Different Foods

Peanuts 1.9%

Beans 2.5%

Sesame 5.3%

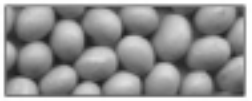


Rice 2.2%

Peas 0.9%

Corn 0-6.4%

Sunflower Seeds 1.9%



Soy 0.1-1.8%

Wheat 1.1-4.8%

Oats 0.8%

Barley 1.0%

IP_6 is in essence a modified sugar molecule that can be bound to a number of minerals. The various B vitamins play important roles in energy metabolism. IP_6's most important role may in fact be in regard to energy, with the other values described in this book such as cancer prevention, only bonuses. Quite the bonus, the bonus of life! In all living cells ATP (adenosine triphosphate) is used to store the energy derived from our food. IP_6 is one of our sources of phosphorus which enables ATP to be formed and thus the energy to be stored. There is debate as to whether IP_6 should in fact be considered a vitamin. See the "IP_6 A Vitamin?" chapter by Dr. Ivana Vucenik, for more molecular detail. This molecule is also a very potent antioxidant. With so much press in recent years, the public now know that antioxidants are good for us. Despite antioxidants being in vogue there is a lot of confusion as to what an oxidant actually is and what role they have in health. See the chapter "IP_6 Super Antioxidant", which discusses these topics and the role of antioxidants as anti-aging medicines. IP_6 affects our health in several ways as you will read and I expect scientists to uncover even more benefits in the coming years as the intricacies of this amazing molecule are revealed.

IP_6 in our food or IP_6 as a Supplement?

Prior to entering Naturopathic Medicine I believed that optimum nutrition could be achieved with diet alone. I felt strongly that the less processed a food the better. At the time I simply didn't think that purified nutrients in capsule or tablet form were necessary. After all I thought concentrated food extracts still had to be processed. A Naturopathic medical education and 10 years of practice have swayed my bias. I'm able to see the beneficial effects of various extracts daily in my patients. I've come to realize that eating optimally is very difficult for many. Families with children, business people and the elderly etc, often don't have the time or aren't able to eat as well as they might like. Our culture itself may be the main villain. We simply don't have time. Fast food is simply that, fast. In 1980 I was taking a marketing course and fast food was the topic. I learned that one of every eight meals eaten in America was from a fast food establishment and that the prediction then was that eventually it would be one of every three. YUK! I don't know current stats, but hopefully we have fallen far short of the predictions. In addition our food is often nutrient depleted or contains additives such as hormones or antibiotics.

I was able to witness first hand the impact quality food could make with my mother and her cancer. I saw how her physical being was literally transformed. How eating raw liver daily turned her from someone who was chronically fatigued into someone with a lot of energy. Liver is perhaps an extreme example, but organic raw calf liver extract with the cholesterol & bile removed is now available commercially in a softgel capsule, which means: no taste and no smell. The capsules, which are just a bit more "socially acceptable"

are available from the company: Enzymatic Therapy see www.enzy.com. What my mother would have given to have these capsules as an option.

Years ago, to take advantage of the preventative qualities of IP_6, I would have suggested eating foods rich in IP_6. As a therapeutic cancer agent however, I would have still recommended the supplemental form, since one would have had to consume such large amounts of IP_6 containing foods, that it would be very difficult without dramatic lifestyle changes.

Aside from my personal bias there is a far more important reason to use IP_6 in supplement form. In food IP_6 is bound to protein. For IP_6 to be absorbed it must first be freed from the protein. An enzyme called phytase that is present both in food as well as our intestine performs this function. The problem is that the power of the phytase enzyme damages the IP_6 itself. This renders much of the IP_6 inactive and therefore less effective, so we don't get its full benefit. Pure IP_6 on the other hand is absorbed intact providing us with its complete medicinal properties. Indeed research has proven just that: when fiber from AllBran was added to the diet of rats with mammary cancer, it was much less effective than the equivalent amount of IP_6 added to the animals drinking water.

The scenario can be likened to that of lycopene, which is a potent antioxidant derived from red colored pigments found in fruits and vegetables. The bioavailability of lycopene is greatly enhanced once it is processed using heat or is simply cooked. Tomato sauce or juice for instance supplies far more lycopene than the equivalent amount of fresh tomatoes. There seem to be a few instances when technology can augment nature's healing powers rather than lessen them and IP_6 potency is one such situation.

Cancer Prevention

Prevention is the greatest of all cures. Why is this simple concept so difficult to grasp! I understand as individuals that most of us don't like to even think of cancer if we don't have to. However, why can't medical and government regulators promote preventive strategies? Governments produce anti-smoking campaign posters and publish statistics on one hand, however they have their other hand out looking for tax dollars from cigarette sales. A mixed message and a lack of leadership? Absolutely! As much as I don't like to admit it, insurance companies by charging a premium to smokers may in fact be affecting behavior more than our governments.

When I was a student I remember reading in a conservative medical text book that stated 50% of cancers were diet related and 30% were due to smoking. Yet have you ever heard that 80% of cancers may be preventable with life style changes? What the heck is our government doing! Instead what I constantly hear is: "Please donate to help us win the war against cancer" or "Donate to help us find a cure". Why should prevention take the backseat to a cure?

How are these for sobering statistics? In 1921 some estimates suggest that one in eleven persons got cancer. Today it's approximately one in three! A recent report (April 2004) by the Canadian Cancer Society indicated that cancer was poised to overtake cardiovascular disease as the leading killer of Canadians. Cancer is already the number one cause of premature death. The report stated that in the next two decades as our population ages, the cases of cancer diagnosed annually are expected to increase by a whopping 60%. The fact is we are losing the war on cancer and more importantly, **we're all at risk!**

These numbers are more than sobering, they're SCARY! As a parent I feel it's my absolute obligation to protect my children from danger. How can we sit idly by when our children are mortally threatened? Still most of us do. Why? It's not apathy when it comes to our kids, I think it's simply a case of not realizing there's something we can do.

We're constantly reading about the discovery of a new gene that increases the risk of a particular cancer or disease. Much of this research is performed by our brightest scientists. Yet I feel that for the most part, their efforts are misappropriated and their talents underutilized. I feel these researchers are simply looking in the wrong place. A very strong statement, but ask yourself this question: Is the increase in cancer incidence due to genetics? Of course not! I've heard what I believe to be credible sources, indicate that only 5 to 10% of cancers have a genetic origin. If these statistics are accurate and even if scientists discovered an incredible method by which to avoid all the genetically based cancers, then we would still be dealing with the remaining 90 to 95% of cancers. Could we save more lives if we focused on prevention utilizing what we already know? Yes, without question!

The irony reminds me of a discussion I had in a jungle in Thailand while on vacation several years ago with a visiting researcher and his group from California. They were in Thailand to research the drastic decline in wild tiger numbers. They were employing the same guide as I was because prior to being involved in ecotourism, the guide was a renowned tiger hunter. It was strongly believed that the tiger numbers were quickly dwindling due to poaching as tiger bone is used in Chinese Medicine for arthritis. Since I was studying traditional Chinese medicine at the time I was keenly interested. The researcher was telling me how investigators found tiger bone in several of the herb shops in Hong Kong and that they must find a way to curb the poaching. I got excited, for I believed at the time (and still do for that matter) that I knew how to save the tiger. People in pain will seek a solution. The answer was obvious I thought, offer relief to those in pain. I had lectured extensively about glucosamine and its role in arthritis management. It occurred to me that the way in which tiger bone worked was likely similar to the way that glucosamine worked, which was to supply the nutritional components needed to make cartilage. Healthy cartilage prevents calcium buildup in joints and for many prevents or reduces the pain of arthritis. As glucosamine had just been introduced to North America by way of Italy, I reasoned that it was very likely that the Asian herb shops were not aware of it yet. I thought if herb shops only knew that there was an alternative that worked well, likely by the same mechanism, wasn't expensive and didn't threaten the tiger population, then logically they would switch. The tiger would be saved! My enthusiasm was soon dampened and turned to frustration and anger. This researcher didn't want to hear about glucosamine the "Tiger's Savior". He reasoned that it could affect his research grants. How absolutely pathetic, I thought.

The problem is that cancer researchers are often in the same boat. They need jobs. They need research grant money. A research scientist's career is often judged on the basis of the research grants that they are able to attract.

The problem as Dr. Shamsuddin has discovered is that the field of disease prevention is without glamour and a lack of glamour means a lack of funding.

Finding a cure or better treatment will always garner more attention. A news headline that reads: "New Cure for Breast Cancer" would likely make the front page and the evening news. An article entitled: "Researchers discover eating Brown Rice daily decreases Breast Cancer Incidence" would likely only be found in the health section if at all. Prevention is simply less exciting. In sports such as football or hockey for instance, we're far more likely to remember the offensive stars who do the scoring and not the defensive players who prevent the scoring. Still a lack of media hype is no excuse, medical institutions and governments should realize the human and financial benefits of preventive approaches. In Canada a few years ago for example, the amount spent on osteoporosis treatment was reported to be almost 100 times more than was spent on prevention. The government could literally supply vitamin D, calcium and magnesium for the entire population for less than they spent on treatment.

Obviously we need both prevention and treatment, but the cost savings of preventive measures somehow mysteriously doesn't weigh heavily in decision making models.

Boring as it may seem to regulators, the cancer preventive value of Inositol + Cal Mag IP_6 is surely one of the most exciting developments ever in cancer prevention. Dr. Shamsuddin knew the implications of his experiments. Even though a major government institution such as the National Cancer Institute (NCI) has been made well aware of the tremendous potential, little has come of it. Dr Ivana Vucenik describes the NCI experience in another section of this chapter.

Dr. Shamsuddin initially designed animal experiments to test the hypothesis that it was the IP_6 in the fiber of grains that prevented colon cancer and not the fiber itself. The first experiment was successful enough to further encourage him to keep investigating. Dr. Shamsuddin's first experiment was able to demonstrate that IP_6 in the drinking water resulted in fewer and smaller tumors. Perhaps the most interesting result of the first experiment was that the rate of cell division (mitotic rate) was normalized in the non cancerous tissue. The agent that was used to induce the cancer (carcinogen) normally results in all the cells dividing at a very fast rate of which some of the cells then mutate and become cancerous. In the group of rats that received the IP_6 somehow the cells (both cancerous and non cancerous) were resisting the stimulus to divide rapidly.

The second experiment was designed differently. Instead of providing IP_6 prior to the administration of the carcinogen as in the first experiment, it was provided afterwards. Some of the rats received IP_6 two weeks after the carcinogen was given and some as late as five months after the tumor causing agent was administered. Again the rate of cell division was normalized. Only 10% of the animals receiving IP_6 developed tumors versus 43% that didn't receive it. Even the rats that received the IP_6 five months later received protection, by which time they normally would have already developed tumors.

Protection received after carcinogen exposure is very important as it potentially means that it is never too late to consider prevention. How about smokers who may have smoked for 20 or 30 years? Many of these long time smokers feel that they have abused their lungs for too long and leave their fate to chance. Hopefully now they will have a reason to be proactive. In the earlier inositol chapter you saw research performed by Dr. Lee Wattenberg and others demonstrating protection specifically against lung cancer. In 2002 there were 155,000 lung cancer deaths reported in America. Lung cancer is fatal 85% of the time.

The third experiment by Dr. Shamsuddin was designed to determine if the dosage of IP_6 makes a difference. Perhaps only a little IP_6 was needed and that after that no more benefit could be achieved or maybe the benefits of a small dose could be negated by a large dose? The results showed that yes indeed dosage was very important. It was found that the higher the percentage of IP_6 in the animal's drinking water, the greater was the protection, with a resulting lower incidence of cancer.

It was very early on in the research, but think of how excited Dr. Shamsuddin and his colleagues must have felt. What if IP_6 could do the same in real life for humans as it did in the experiments with animals? Was the reason for the huge difference in colon cancer rates between the Finns and Danes due to the IP_6 content in the grains as Drs. Graf and Eaton had proposed? Colon cancer is the third most common and second most deadly cancer second only to lung cancer. The American Cancer Association reported 130,000 new cases of colon cancer in the year 2000. The reality of IP_6 being fiber's secret ingredient was starting to look more and more likely. Was the missing link being revealed? Could IP_6 result in 75% fewer colon cancers as in the experiments? Only time will tell, but remember the Finns had half as much colon cancer while consuming less fiber, however their fiber was rich in IP_6.

A highly significant study due to the large number of cancer patients was conducted in Italy between 1983 and 1996 by Chartenoud et al that investigated the incidence of all cancers. The researchers studied a total of 10,149 cancer patients and 7990 patients without cancer. Their conclusion was: “High intake of whole grain foods consistently reduced the risk of neoplasms of all sites, except thyroid.” In other words, whole grain consumption lowered the risk of almost all cancers. It’s most important to be clear that the authors referred to whole grains and not simply fiber. A similar observation was reported by Drs. John Higginson and George Oettle of South Africa in 1960. They reported that the Bantu people had approximately half the incidence of all cancers and only a tenth of the incidence of colorectal cancer (The word Bantu is used to denote black Africans from various tribes and is not referring to a people from a specific tribe). They reported: “A high incidence of large bowel cancer has yet to be reported from a community living on simple, unspiced, natural diet....In the Bantu a large amount of roughage is normally consumed and constipation in the Western sense is rare”.

Yes you read correctly, 90% less colon cancer in the Bantu! Now these numbers reflect a true winning of the war on cancer. Can you imagine the elation, admiration and perhaps resulting Nobel prize should a research team discover a cure for colon cancer that worked 90% of the time. Most importantly, evidence was presented that the incidence of almost ALL cancers can be reduced. People don’t believe that they can make a difference and governments haven’t told us so. People don’t realize that a lot of the cancers can be prevented. Sadly, some people have come to the conclusion that cancer is almost a normal consequence of aging. It’s not! I feel if we empower people with information on how to prevent cancer, that we will have far more impact on the war on cancer than all the genetic engineering or chemotherapy that has ever been developed.

Cancer Treatment

Given the choice any sane person would choose prevention to treatment when it comes to cancer. Unfortunately many of us don’t have the option to choose.

I strongly believe that a combined approach offers the best hope for cancer patients. As I was writing this chapter, I saw an ad on TV by the Cancer Treatment Centers of America. Hats off to them for having the courage to openly state that their patients are evaluated and treated using the best of both western and naturopathic medical approaches.

Typical Western Oncology

- Remove cancerous cells by surgery
- Destroy cancerous cells with chemotherapy and/or radiation

Typical Naturopathic Adjunctive Support

- Support the patient and address any other chronic or acute health concerns.
- Optimize nutrition-Many cancer patients die not of cancer, but of starvation as a result of a very diminished appetite or impaired digestive function or both.
- Immune Support-There are several useful natural immune stimulating herbs and nutrients. Please note that unfortunately immune stimulation is also how many cancer patients get taken advantage of, as exaggerated or completely false claims are often directed at these vulnerable patients.

Evaluating a situation from different perspectives allows for a greater number of treatment options. Medical oncology focuses on the cancer usually utilizing surgery, chemotherapy and radiation. Naturopathic medicine typically focuses on the patient. If other aspects of a cancer patient's health are optimized, they should logically be able to mount a better resistance. In addition to overall patient health, naturopathic medicine often employs immune stimulating approaches. Surely an approach that encompasses a way to destroy cancer cells at the same time as it promotes overall health and boosts immune response would offer a patient a better chance than simply attempting to solely remove or kill cancer cells.

In the early 1980's Dr. Shamsuddin published papers that suggested the health and visual state of the cells lining the colon may have predictive value when it came to assessing the risk of developing colon or rectal cancer. This concept would seem intuitive to a physician practicing holistic medicine. This hypothesis is another way of stating that the health of the whole (colon) is reflected in the health of the parts (crypts). Crypts is simply a term used to describe the physical shape of the intestinal lining. The intestinal lining or mucosa is organized into a series of little pockets or folds which increases the surface area and as a result increases the food absorbing capacity as well. Cancer typically just doesn't appear spontaneously. There is usually a set of conditions that causes and enables cells to survive a series of mutations. Prior to this, the focus on colon cancer research was the investigation of polyps and their potential transformation into tumors.

For his hypothesis Dr. Shamsuddin was severely criticized. An associate editor, Robert R. Pascal, MD of the peer reviewed journal "Human Pathology" had these words in reference to a paper Dr. Shamsuddin published in 1981. "The therapeutic implications of the article are dangerous and represent a threat to both the health of patients and the credibility of diagnostic pathologists." I never cease to be amazed at how ideas that seem to be logical in medicine are so strongly refuted. It's a wonder at times that progress is ever made. Today the atypical mucosa or crypts that Dr. Shamsuddin originally described are now the standard markers used in colon

cancer research…..the only difference is that they are now called "aberrant crypts".

Due to his advanced understanding of the physiology of colonic crypts and the cells within, Dr. Shamsuddin was able to invent a test with the distinction of being able to detect colon cancer in its earliest stage. This is truly a major contribution in the field of medicine. The test will likely result in the saving of tens of thousands of lives (if not more) annually, as colon cancer is often found only after it has spread. The test is now being investigated for its potential to be used in other cancers. Many types of cells (colon, lung, prostate or breast etc) secrete sugars that are needed to make up our normal mucus or mucin protective coating. Cancerous cells secrete an additional abnormal type of sugar, which the test simply and inexpensively identifies. See the last section of this chapter by Dr. Ivana Vucenik for details on the tests or visit the website www.imimedical.com and see the LungAlert or ColorectAlert tests.

By now you may have come to the conclusion that I am a huge fan of Dr. Shamsuddin's medical contributions. It's true, but I mention his other discoveries here because they are so relevant to cancer treatment. I also mention them because discoveries that allow us to take a step forward are often criticized or worse, simply overlooked.

As previously mentioned, scientists had contemplated phytate as having cancer preventive qualities. To his credit Dr. Shamsuddin carried out research to test the hypothesis. The ability of IP_6 to control the rate of abnormal cell division was truly an unexpected and amazing finding. In the experiments the rate of cell division was sped up using carcinogens. Somehow the surrounding healthy cells resisted the stimulus from the carcinogen and behaved or divided normally. Dr. Shamsuddin was especially intrigued by one of his earlier experiments in which the animals received protection even though the IP_6 was administered 5 months after the cancer causing agent. At the five month point the animals would have already had cancer in many cases. What was happening? Was the IP_6 having a therapeutic action as well? Was it possible that the same medicine that was preventing cancer was also treating cancer? What a blessing if true!

To investigate Dr. Shamsuddin designed further experiments. In the first study mice were inoculated with fibrosarcoma. Once the cancer had taken hold the mice were then injected with IP6. The mice receiving the IP6 had smaller tumors, fewer metastases and survived longer.

Utilizing the cancer screening tests invented by Dr. Shamsuddin, a number of researchers have been able to demonstrate that colon cancer cells "behave" or express themselves in a more normal manner when exposed to IP6. Even though the cells have altered DNA or genetics, researchers discovered that the cells produced very little or any of the sugar that is unique to cancer cells. See the website www.ip6.info for colored pictures of this and other experiments.

This may sound like obscure researcher type info, but it is highly significant. So much of our research is directed at identifying gene sequences, but health or disease is often far more dependent on how we express our genetics than the exact genes themselves. In medicine identical twins that are separated at birth and live with different families are often studied in order to investigate how various sociological and nutritional factors etc. affect the expression of their genetics. With rheumatoid arthritis (RA) for example, it is rare for both separated twins to have RA, even though they have exactly the same genes. In other words the identical twins (one with RA and the other without) are examples of two different expressions for the same set of genes.

With the colon cancer cells investigated for sugar production, both the control and treatment group of cells originated from the same culture, so they have the identical DNA or genes. In addition to the previously discovered ability to normalize the rate of cell division, IP6 was now proven to normalize the sugar production of these cancerous cells. This is another example of altering the gene expression towards a more healthful state. The proven ability to change cancer cell physiology has major implications. Cancerous cells that "behave" have far less impact on our health. When it comes to cancer, few researchers have considered taming or controlling the condition; instead, most are focused on killing or destroying these cells by way of immune augmentation, radiation or chemotherapy etc.

A very practical aspect of this discovery is akin to the following scenario, which is not uncommon: A person has been screened positive for cancer and the cancer has been removed. He/she has a high chance of recurrence and is now placed on preventive dosage of Inositol + Cal Mag IP6. Should Inositol + Cal Mag IP6 effectively prevent the recurrence, subsequent routine screening should continue to test negative.

IP6 has been proven to boost Natural Killer (NK) cell activity. NK cells are white blood cells that specifically target virally infected and cancerous cells with the intention of destroying them. The importance of the previous test was that it was performed in a Petri dish. The Petri dish contains no immune or white blood cells, so that the value of IP6 cannot be attributed to an augmented immune response. These experiments provided further evidence that IP6 directly affects the physiology of the cancerous cells.

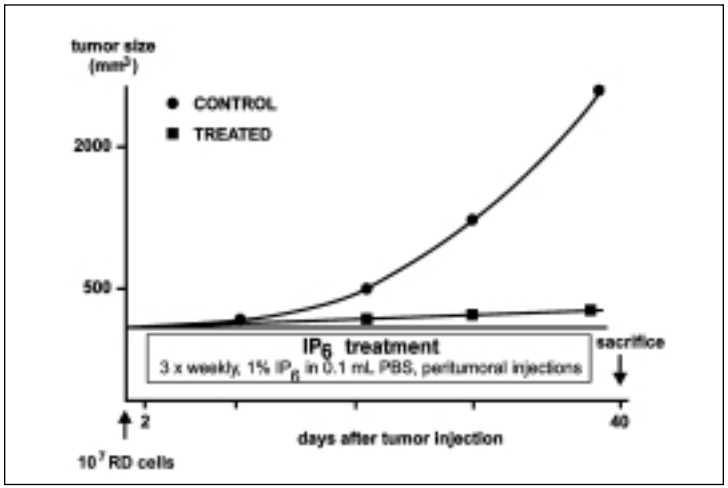
Medicines become especially valuable when they are able to help overcome genetic predispositions thus leading to healthful states. Unfortunately, far too many people believe that genetics are the root cause of many of their ills and worse, often feel that there is really nothing they can do. Often I have heard patients say that their father and grandfather had early heart attacks and that they probably will also, or that their mother and sister had breast cancer so they'll likely be a victim as well. Hogwash! If you were to trace those same genetics back a few more generations to when a more primitive diet and less stressful lifestyle were the norm, you would probably find different results. American Indians and African Americans have a much higher risk of diabetes. Go back 100 or 200 years and this wasn't the case. Their genetics haven't changed much, so why now and not then? The answer can be found in today's current diet and lifestyle.

Many types of cancer cells have been tested to evaluate their response to IP6 in a Petri dish. The result has been several positive cellular changes to their physiology, including the most important, which has been the ability to normalize the rates of uncontrolled abnormal cell division. The results can be considered similar to chemotherapy in the sense that by the end of the experiments there

are a contained number of cancer cells. Chemotherapy kills most of the cells, but the ones that survive continue to divide rapidly. IP6 on the other hand is non toxic and doesn't kill the cancer cells, except at high dosages. IP6 slows or normalizes their rate of division so that by the end of the experiment you don't have nearly as many cells as you would expect.

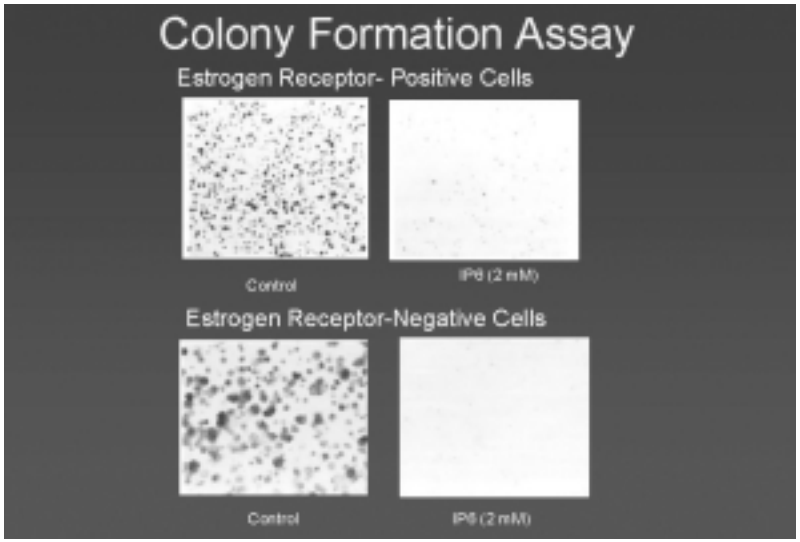
There are literally dozens of very well designed studies investigating the effects of IP6 on several common types of cancer. Below are a few of the studies, chosen to highlight some of the potential benefits and mechanisms of action of this simple rice extract.

Rhabdomyosarcoma (RD) is a common tumor of young people. It is very aggressive and if spread or metastasized usually doesn't respond to current therapies. In other words, it's deadly. To test the effect on RD, mice were inoculated with RD cells and then treated with IP6. After 5 weeks the mice that did not receive IP6 (control) had tumors that were on average 49 times larger than the treated animals that did receive IP6. In addition to a phenomenal suppression of tumor growth, the IP6 treated mice also showed better cell differentiation. See the following graph.



6b.1

If we maintain the premise that IP6 should be useful in most if not all cancers, then hormone sensitive cancers should respond in a similar fashion to non hormone sensitive cancers. To test this line of rationale, breast cancer positive (MCF-7) and breast cancer negative (MDA-MB 231) cell lines were compared. The results were indeed similar. As you can see from the slides, the colonies of both estrogen positive and negative breast cancer cells were smaller and fewer in number when they received IP6, versus the control cells which did not receive IP6.



6b.2

Another test was performed to see if the breast cancer cells would mature in a manner similar to the colon cancer cells previously mentioned. The breast cancer cells treated with IP6 were fewer, were better differentiated and had a darker orange pigment or color. The dark orange indicates lactalbumin production. Lactalbumin is secreted by breast cells once they have reached a certain degree of maturation. The untreated cells are dividing too quickly and as a result don't mature or express lactalbumin. Again please see the website www.ip6.info for details of the experiment.

Very significant breast cancer research with IP_6 was carried out last year (2003). The scientists wanted to know if IP_6 would influence the effectiveness of tamoxifen or adriamycin, which are commonly used breast cancer drugs. The drugs were tested alone or in combination with IP_6 on 3 types of breast cancer cells; estrogen positive, estrogen positive cells that were adriamycin resistant and estrogen negative cells. In addition to confirming prior reports that IP_6 alone inhibited the growth of breast cancer cells, the data showed that IP_6 acted synergistically with both drugs, increasing their effectiveness and did not increase the drug toxicity. The combination of drug and IP_6 was particularly effective against the estrogen negative and adriamycin resistant cells, which generally do not respond as well to treatment. The research carries the implication that the effect of conventional chemotherapy may in fact be augmented with the adjunctive use of IP_6.

Cancers are often monitored by a number of blood tests, depending on which cancer a patient has. A blood test for liver cancer is called Alpha Feta Protein (AFP). The amount of AFP in the blood indicates how active a liver cancer is. From the results below you can see that the value of alpha feta protein was dramatically influenced by IP_6! The control, which received no IP_6 had AFP levels of 1379 ng/ml versus the 1 mM group which had AFP levels below 2 ng/ml. This is yet another example of normalized cellular activity from a cancer being exposed to IP_6.

Effect of IP_6-treatment of HepG2 Cells on AFP Secretion

Treatment	AFP secretion in culture media (ng/ml)	AFP secretion (pg/cell)
Culture media	1379.0 ± 65.7	27.6 ± 1.3
0.25 mM IP_6	275.5 ± 44.6	10.2 ± 1.7
0.5 mM IP_6	63.0 ± 24.0	5.3 ± 2.0
1.0 mM IP_6	1.9 ± 0.2	0.3 ± 0.0

Control *vs* treated $p < 0.0001$ (t-test)

Anticancer Res, 1998

6b.3

There is a valid criticism that IP_6 research has generally been performed on human cancers that were transplanted into animals or onto petri dishes. Clinical studies with people are now starting as a result of the solid foundation of scientific evidence that is now available from research labs from around the world. Human clinical trials take time, time that cancer patients often do not have. Determined researchers from several countries are now involved in IP_6 research because of the huge potential for this completely novel approach to diminish human suffering. Involved because research results (as above) have been almost miraculous. Involved because the proposed mechanisms are novel and provide cancer patients a true ray of hope. Involved because too many patient testimonials are defying expected patient outcomes. When I was a Naturopathic student in the eighties, it was estimated that the cost to get a new drug approved in the United States was $300 million. Current estimates are in the billion dollar range. The supposed safety of IP_6, as it is already part of our food supply has enabled human trials to begin. Had IP_6 been a synthesized or man made molecule, trials would

probably still be a few years off and the eventual price to patients would likely be in the thousands, if not tens of thousands in order for companies to justify the development costs. There are typically pros and cons with any system of administration or regulation. For IP_6 the pro is that it is available sooner rather than later and at a fraction of the cost. The downside is that not being a new synthetic molecule there is little financial incentive for drug companies to investigate Cal Mag IP_6. As a result research depends upon scientists who strive more to make a difference rather than strive to make a living.

As cancer can kill, our first instinct is to fight these aberrant cells. However, when we step back and think about it, we already know that several forms of cancer can exist in us for years before being detected or causing symptoms. Most breast and prostate cancers for example are normally very slow to develop and are often present for up to a decade before diagnosis. We can live with cancer. Many of us already are and don't know it. The fear of cancer has led to search and destroy treatment strategies. Inositol + Cal Mag IP_6 offers a completely novel approach, but it will take a while for acceptance, as the concept of allowing cancerous cells to mature is counter intuitive for most of us. However, cell maturation takes time. Time we can use to mobilize our immune system, time to improve other aspects of our health, time for other therapies to take effect.

How IP_6 Protects Us Against Cancer

There are several ways in which IP_6 is known to help in the prevention and fight against cancer. The phosphorylated inositols are very common intracellular messengers, which means they control and influence many cellular activities. As intracellular messengers, I fully expect that additional mechanisms will be described in time, as our understanding of cell biology advances. A brief summary describing what is presently known about how this rice extract works is below.

1-Helps to normalize the rate of excessive and uncontrolled cell division
2-Helps to normalize cell physiology
3-Natural Killer (NK) cell enhancer
4-Supports tumor suppressor gene activity
5-Inhibits inflammation
6-Potent Antioxidant
7-Enhances apoptosis, which is a natural programmed cell death
8-Antiangiogenic effect, which is the inhibition of new blood vessel growth
9-Inhibits metastasis

Normalizes the Rate of Cell Division

Cancer cells are generally considered to have lost their control mechanisms and as such typically divide too rapidly, resulting in a

great numbers of cells that can have a devastating impact on health. IP6 somehow amazingly helps to slow or normalize the rate at which cancer cells divide. This is such a dramatic finding that it may in fact cause us to rethink our concept of cancer, as it is reestablishing control in cells that by definition have lost their control mechanisms due to gene mutation!

Helps to normalize cell physiology

How a cancer cell expresses itself largely determines how fierce a battle a patient may be facing. Again, experiments have shown IP6 normalizing several aspects of cell physiology in spite of the fact that these cells have altered DNA. Examples of normalized physiology from previous chapters included lactalbumin secretions from breast cancer cells or a return to normal sugar production in several cell types. In time scientists will likely find out how this occurs. This reminds me of aspirin. Until very recently we didn't know how aspirin worked as a pain reliever, instead we only knew that it did for over a hundred years!

Natural Killer (NK) cell enhancer

Natural killer cells are white blood cells that help to protect against virally infected and or cancerous cells. Some researchers believe that the higher the NK activity, generally the lower will be the incidence of some cancers. See the "Immune Support" chapter. NK cells help to prevent the establishment of tumors from cancerous cells. It has been estimated that healthy adults produce 500 to 1000 cancer cells daily. NK cells and programmed cell death (see apoptosis below) result in the vast majority of these cells being destroyed and removed. During times of stress our NK cell activity is often compromised. NK cells have a greater role to play in the prevention of cancer, but are also important when our immune response is limited during and after stressful occurrences. Cancer patients will sometimes say that they felt that an existing cancer that was thought to be under control, suddenly started to grow or spread after a very stressful period. Unfortunately NK activity is often "Over Promoted" when it comes to treating an existing cancer. The internet

is full of NK cell boosting products that have either misleading or sometimes entirely false claims of health benefits that are targeted specifically at cancer patients. While a decrease in NK-activity is believed to go hand in hand with an increased risk for certain cancers and *vice versa*, this concurrent activity for any compound must be demonstrated; one must therefore carefully look for this proof for any so-called NK boosters. Fortunately, you can feel assured that the claims regarding Inositol + Cal Mag IP6 are credible. See the immune chapter for a graph demonstrating the effect of natural killer cell activity on cancer incidence.

Increases tumor suppressor P53 gene activity

Our DNA or genetic material contains tumor suppressor genes. These genes inhibit pathways or processes that allow cells to become cancerous. The p53 gene acts as a "policeman" by preventing genetically damaged or cancerous cells from growing and propagating. If the p53 gene becomes damaged or compromised, then cancers can establish themselves much more readily. IP6 has been shown to greatly increase the amount of the p53 gene (up to 17 times in some experiments). Tumors are known to be more resistant to chemotherapy when p53 expression is low. Alternatively, when used together with agents that increase p53, standard chemotherapeutic agents are known to be more effective. This may explain in part why the effects of tamoxifen and adriamycin are augmented against breast cancers when IP6 is added.

Inhibits Inflammation

The level of systemic inflammation is now being considered when estimating a survival prognosis. Inflammation results in the release of cytokines. Cytokines are chemical messengers which trigger reactions that enable normal cells to grow and repair themselves. They can also cause cancer cells to grow. Other anti-inflammatory agents such as Cox2 inhibitors are now being researched for their use in cancer therapy. IP6 has been investigated for its anti-inflammatory effects in diseases other than cancer, but the ability to reduce inflammation may in time prove to be very significant.

Potent Antioxidant

IP_6 is a potent antioxidant that protects our tissues. Antioxidants are becoming very popular as they are now known to protect us from various disease states and aging in general. As far as cancer is concerned, oxidative damage to our DNA leaves our cells susceptible to mutation that can result in cancerous cells being produced. In comparison to green tea, which is a well known antioxidant and believed to play a significant role in the longevity of the Japanese, IP_6 is much more potent.

Enhances apoptosis, which is a natural programmed cell death

Programmed cell death is orderly and results in the removal of individual cells without affecting the surrounding cells. This is a normal part of growth and the maintenance of healthy tissues. It's an ideal way to remove unwanted cells as no inflammation or immunological reactions result. Cancerous cells are less able to undergo normal cell apoptosis. IP_6 has been shown to enhance this natural process.

Antiangiogenic effect, which is the reduction in new blood vessel growth

Tumors require blood vessels to be created in order to deliver nutrients to these rapidly dividing cells. By inhibiting this process it is theoretically possible to "starve" cancer cells. Cancer cells can have up to 30 to 40 times the metabolic rate as normal cells and as such may require a tremendous amount of oxygen and nutrients. IP_6 has been shown to inhibit tumor blood vessel growth in a number of studies. See the website www.ip6.info for the pictorial results of antiangiogenic experiments.

Inhibits Metastasis

IP_6 inhibits the adhesion of cancer cells to the extracellular matrix proteins, thereby leading to an inhibition of cell migration and invasion. Limiting adhesion is an important aspect, especially after surgeries and biopsies, as the various procedures can cause cancer cells to become dislodged. Treating multiple tumor sites is more complex, so strategies to limit cancer spread need to be incorporated.

As you can see there are several important ways in which IP_6 can protect us against cancer. Presently pharmaceutical companies are looking to develop drugs to treat cancer utilizing the mechanisms above. Unfortunately it's very difficult because many of the substances being tested are newly created molecules, having never appeared in nature before. As a result severe side effects are common place. On the other hand this natural supplement already exists in all of our cells, so side effects, if any, are rare.

THE POLITICS OF CANCER RESEARCH

Dr. Ivana Vucenik Ph.D.

Political and financial realities of cancer research can hinder advancement. Dr. Shamsuddin's efforts have always been considered controversial. Even though his research has been profound and enlightening, the sheer simplicity of his insights should have prevented controversy. Unfortunately, this has never been the case.

As a research hematologist (I study the workings of the various cells that make up the blood) I had been researching natural killer (NK) cells. Dr. Shamsuddin was also investigating NK cells in relationship with IP_6. I began to work with him in 1989 and have worked on this project ever since. Working in unchartered waters is often difficult, but the implications of the work have supplied more than enough motivation. At the same time the National Cancer Institute (NCI) has provided a few road blocks to keep things just a little interesting.

As you know, fundamental to any cancer prevention is early detection, preferably even before it has formed; for if the cancer is already formed, it is too late to prevent it.....it's there! And that calls for treatment, not prevention. Once a person is identified to have a pre-cancerous condition or have high risk for cancer due to family history, life-style etc., then we have to give him/her prophylactic or preventive therapy. Dr. Shamsuddin's efforts in cancer research have been directed to both. By now you have gathered that he is the pioneering scientist to show that Inositol + Cal Mag IP_6 is anti-cancer;

but his first experiments were on inventing a simple, reliable and an inexpensive test for screening for cancer, using colon cancer as a model.

The Cancer Screening Test

Many questioned his sanity, for in this arena too, he went against conventional wisdom and dogma. Thus not surprisingly, a fellow scientist who has been a member of "Study Section" [a group of peer scientists who grade grant applications] sardonically told Dr. Shamsuddin that his applications on cancer screening tests and the anti-cancer compound (Inositol + Cal Mag IP6) provide much needed entertainment to otherwise boring review sessions: **" the same guy has found a test and a treatment for cancer?! Ha...Ha.. Ha".** This quote as pathetic as it sounds, illustrates what can happen in the world of academia; a world full of egos and jealousy, a world where scientists are often judged solely by their contributions. A world where a breakthrough is often judged and then held back by those who haven't yet made their own mark, a world where genuine innovation or scientific breakthrough can be perceived as threatening.

It has been, and continues to be a dogma amongst scientists in the field of colon cancer that colonic polyps are pre-cancerous, a fact Dr. Shamsuddin does not dispute. But the disagreement is in regards to the likelihood of polyps becoming cancerous, i.e., what percentage of polyps mutate further and turn into colon cancer? This is crucial, for if most of them do, then the practice of routine colonoscopy to remove these polyps is certainly justified. The current day practice in screening colon cancer is to perform a fecal occult blood test which is **notoriously inaccurate.** If a person has a hemorrhoid or is taking aspirin etc, the test can be positive due to the presence of blood. If on the other hand a cancer is actually present, but not bleeding, then the test results may show up negative. The terrible reality is that thousands of colon cancers are missed each year due

to the limitations of this test. If a person is positive, he/she usually undergoes a colonoscopy. Most of the time a benign polyp is found and if the person is over 50, then they are asked to come back for routine follow up. One could be cynical and suggest that a certain group of physicians and corporate entity might want to keep the polyp story alive along with an unreliable screening test [if it can be so called] for it provides financial benefit to both.

In1975, Dr. Shamsuddin started his experiments. He investigated how colon cancer forms in rats and mice and induced cancerous changes to rat and human colon cells kept alive on Petri dishes in the laboratory. As a Board-certified [human] pathologist, he painstakingly analyzed the cancerous and non-cancerous colons of both humans and experimental animals. He found that the vast majority of polyps do **not** become cancerous over a very long period of time. His research indicated that the majority of colon cancers are not of polyp origin, rather that they begin in the flat lining.

As if that was not controversial enough, in the early eighties he published evidence that the otherwise normal looking colon away from the cancer shows subtle morphological and biochemical changes of pre-cancer and cancer. He therefore felt that information regarding the propensity to develop a cancer could be gotten by evaluating the non cancerous colonic tissue. For this opinion he was again severely criticized. Today, this is actually the foundation for the model utilized in a lot of colon cancer research.

Using a very simple technique he demonstrated that it is possible to predict whether a person has colon cancer or not by taking a rectal mucus sample during routine examination and analyzing it in a very inexpensive manner. The whole process takes less than 10 minutes! Dr. Shamsuddin published these in well respected peer-reviewed scientific journals. The story was written-up in national and international news papers and was on TV in 1987, coinciding ironically with the story of President Regan's colon cancer diagnosis. Companies became interested; at least two US multinational companies and several Japanese companies thoroughly investigated, and despite excellent results, decided to proceed no further even though

the test was far superior to the existing fecal occult blood tests. Why? It seems totally illogical to me, but perhaps the inexpensive nature of the test was unappealing to medical companies. One would think that government agencies and medical companies would have been beating a path to his door. After all, no other effective colon cancer screening test was or for that matter is available even today.

The Chinese however paid attention. By 1995, there were several dozen scientific papers [mostly in Chinese, but some in English] and the colon cancer screening test is now being widely used in China. The test goes by a number of names in China such as: "rectal mucus test", "galactose oxidase test" after a key ingredient, or "Shams' test" after the name of the inventor.

Be that as it may, Dr. Shamsuddin reasoned that if this "field-effect" phenomenon is operative in the colon, it's likely to be in other organs as well. Cancers of lung, breast, prostate, uterine cervix etc., could similarly be screened for in a simple, rapid, inexpensive and pain-free manner. And he proved that to be the case. A Canadian company, International Medical Innovations (IMI) www.imimedical.com has embarked on this and are in the process of bringing these various cancer screening tests to the market place. Two years ago IMI made front page news in one of Canada's national newspapers. IMI reported that the lung cancer screening test "LungAlert™" was the most sensitive (finds the highest percentage of cancers) lung cancer test ever. IMI reported that the big advantage was that cancers could be found when still minute and largely undetectable via x-ray. All patients had to do was cough up some sputum, have the doctor place it on the test strip and wait a minute or two to see if color changes to the test strip occur. Hopefully, we will have the opportunity to benefit from these early detection tests sooner rather than later.

IP6 and the Government

This story is strikingly similar, except that now it involves the National Cancer Institute (NCI).

By early 1987, Dr. Shamsuddin and his colleagues presented data at national scientific meetings showing the striking anti-cancer action of Inositol + Cal Mag IP6. The results were carried by many a print-news media, including the *Washington Post, Associated Press* etc. But then again, nothing happened!

Realizing the enormous potential of Inositol + Cal Mag IP6 in cancer prevention and therapy and having demonstrating the strikingly reproducible results, needless to say, Dr. Shamsuddin was becoming frustrated with the lack of further interest. Insofar as biomedical research is concerned, and cancer research in particular, grant funding is crucial. Unless one's research is supported by grants, there is very little likelihood of continuing the work. Thus, though one can [as Dr. Shamsuddin has] conduct pre-clinical laboratory experiments on a shoe-string budget, clinical trials on the other hand cost hundreds of thousands of dollars, if not millions. Unless government agencies such as the NCI come forward with money, it would be impossible to take any such work to the next level.....the humans. It was in designing and conducting pre-clinical lab experiments that I have spent much of my efforts with Dr. Shamsuddin.

While NCI gives grants to investigators with brilliant ideas, it also earmarks funds for projects that the NCI scientists [project officers] consider to have good potential. Request for applications (RFA's) are published and funds are disbursed to scientists on a competitive basis. As his department head once chided him for his failure to garner NCI funds for his research, he failed to arouse any interest from NCI staff to have funds earmarked for clinical trials involving Inositol + Cal Mag IP6, either in a preventive or therapeutic setting. **It may be worthwhile to keep in mind that for every research dollar awarded directly to the scientist, the institution receives additional 40 cents to ~$1.00 as overhead; thus there is pressure by universities/institutions on their professors to apply for research funding.**

So, he started to write to his local congressman and senators. Senator Paul Sarbanes (D. Maryland) was the only one who not only appeared to have paid attention [he did not send a 'form-letter'], but also acted on it. He asked NCI's Cancer Therapeutic Branch to respond. The Associate Director of the Developmental Therapeutics Branch (ADDTB) responded by stating that NCI had tested IP_6 and found it not to be effective. I found it very interesting and along with Dr. Shamsuddin very frustrating that one **unpublished** report was used as reference, when there are 5 or 6 published papers from NCI scientists that state IP_6 does in fact have an anti-cancer action. That did not stop the process as S. Elizabeth Clay, working with Rep. Dan Burton (R. Indiana) called Dr. Shamsuddin and wanted to hear more about IP_6 and set up a meeting with the Congressman. At the meeting, Dr. Richard Klausner, the then Director of NCI essentially dismissed Dr. Shamsuddin and his work on Inositol + Cal Mag IP_6. Unimpressed, Rep. Burton asked Dr. Klausner to order re-testing under Dr. Shamsuddin's supervision. Please visit:

www3.cancer.gov/legis/sept99/hearings.html
www3.cancer.gov/legis/june99/hearings.html

What happened next was that Dr. Shamsuddin was given the data sheet on the "60 cell" assay showing "negative" results with IP_6 and was told how NCI performed its testing. The "60 cell" assay is a standard NCI uses by which the effectiveness and toxicity of chemotherapeutic agents are evaluated. It was readily apparent that NCI was testing IP_6 at concentrations 100-10,000 fold less than what Dr. Shamsuddin and other non-NCI scientists were using. You could think of it as using a minute amount, such as only 1mg of vitamin C or 1 iu of vitamin E and looking for an effect. Of course the NCI found no effect at such small doses. Most interestingly, at concentrations nearing the dosage used by non-NCI scientists, **59 of the 60 different cancer cell lines were showing reduction in cell growth!** But that's when the experiments were terminated! IP_6 was not killing cancer cells and it was not doing it at a very low concentration [unlike IP_6, chemotherapeutic agents are highly toxic and so only minute doses are used]. I speculate that their logic was something like: if it's not toxic and doesn't kill cancer cells, how could it

be our magic bullet? Furthermore, as opposed to dissolving IP_6 in water [remember, it's a sugar molecule that dissolves in water], NCI scientists were dissolving it in a solvent called DMSO! So Dr. Shamsuddin and I went to the NCI laboratories in Frederick, Maryland with some IP_6 and distilled water and demonstrated to NCI scientists, how to dissolve IP_6 in water! Most importantly, the results on Petri dishes using human cancer cell lines were reproduced. The ADDTB then wanted to test its safety. Mice were given increasing doses of IP_6 orally and even at an extremely high dose, it was non-toxic. But, when given intravenously it became lethal at a certain dose. And that literally killed the mice and the fate of IP_6 as an anti-cancer agent in the eyes of the NCI. So the ADDTB concluded that since anti-cancer agents are usually given by injection and IP_6 kills mice when given intravenously, therefore NCI found no scientific basis to justify continued study of IP_6 for established disease." Just in case you are wondering, as vital as water is to our survival, injecting a large amount of it intravenously will as definitely be lethal! And that's where in terms of the NCI the story ends for cancer treatment. The question is obviously why not just take it orally? At Harvard decades earlier, very high oral doses were used for up to two years to prevent kidney stones with no ill effects.

One is also left to wonder why was it never considered as a preventive agent by the NCI either? Prevention always seems to take a backseat, so I'm not surprised.

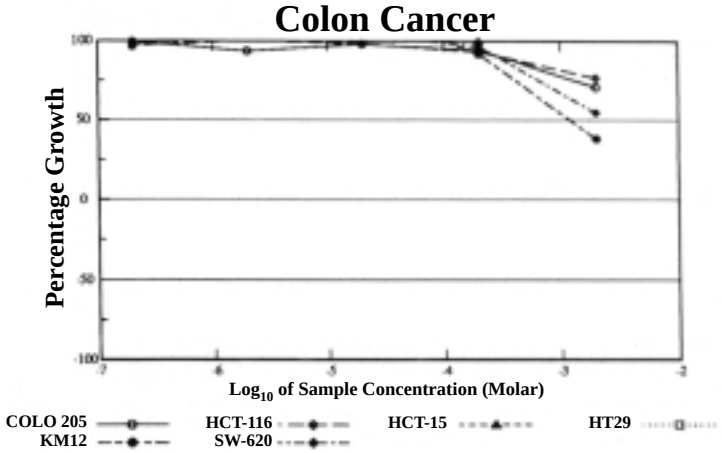
You can see from the following charts how the IP_6 inhibited the various cancers. It's amazing that 59 of 60 types of cancers are inhibited using a non toxic agent. It makes me wonder what NCI scientists see that we don't. What more could they possibly want to justify further study? I wish they'd tell us.

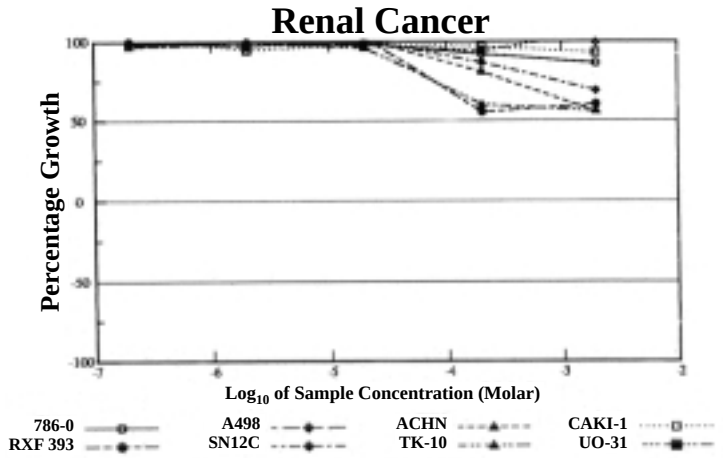
Despite the seemingly illogical discontinuation of interest by the NCI, results ultimately speak for themselves. As such, both Dr. Shamsuddin and myself feel compelled to keep knocking on institutional doors until we receive an audience. Dr. Shamsuddin and I have been published in many of the world's most conservative and well-respected medical journals. In fact the journal *Anticancer Research* dedicated an entire issue to reporting the results of the

Kyoto conference of 1998. I feel it's only a matter of time until exposure in all these academic journals will inspire human trials and we are grateful that this is already happening to some extent.

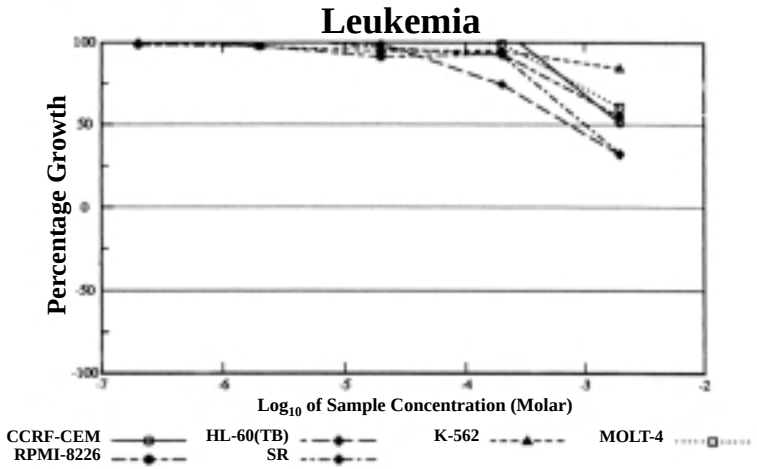
Following are the results from the 60 Cell assay. Of the 60 types of cancers tested, 59 of them showed restricted or inhibited growth as the concentration of IP_6 was increased. The charts are very similar for the various cancers. For demonstration purposes the leukemia, colon, breast and non-small cell lung cancer results are provided below.

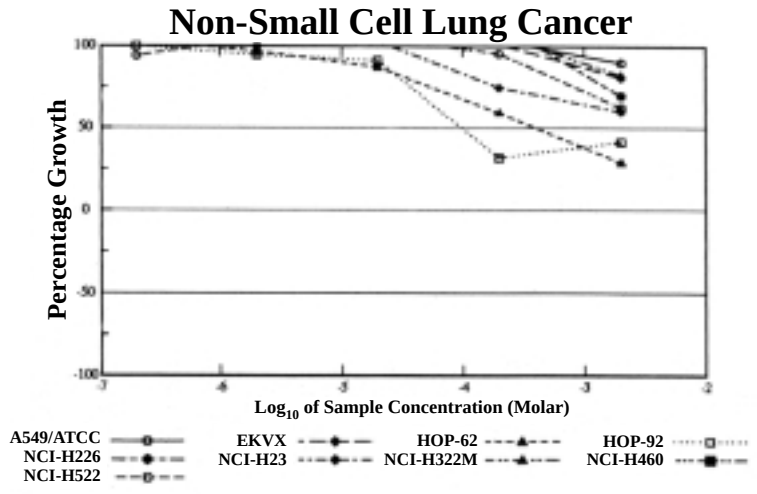
NCI Developmental Therapeutics Program
Dose Response Curves
Test Date April 5, 1999 Report Date April 15, 1999





6d.1





6d.1

Osteoporosis

It's no secret that osteoporosis is at epidemic levels. And with our aging population it's likely to get worse. Women are generally keenly aware of the problem, however many don't realize that half as many men ultimately experience significant bone loss as well. Significant in this case implies that the person has lost enough bone mass that they are at an increased risk of a fracture.

Hip fractures pose a tremendous risk. A large percentage of hip fractures result in death, due to clots from extended bed rest or disrupted blood flow in the area etc. Another large percentage of patients end up requiring long-term care facilities, as many are unable to return home afterwards, since they can no longer care for themselves.

I found a survey from years ago very interesting. The study revealed that women in general were more afraid of osteoporosis than cancer. I believe that this may in fact be true, as many of my women patients ask about bone density, whereas it is me who usually brings up cancer risk.

Digestive health has a major impact on bone density, since it affects mineral absorption. Many people mistakenly think that if they are consuming 1000 milligrams of calcium, that that's how much calcium they are getting. The numbers are in fact far less. Even with optimal digestion, it's estimated that only 22% of the calcium consumed is actually absorbed. With poor digestion the percentage can drop to a mere 4% and this scenario is very prevalent, especially among the elderly. The result is that a person with poor digestion may be absorbing as little as 40 milligrams, even though they are supplementing with a 1000.

A solution to increase mineral absorption is to use minerals that are bound to other molecules. With anemia for example, the absorption of iron ranges from approximately 1% with meals to 3% on an empty stomach. However, if you get your iron from protein, then the absorption can increase dramatically. Clinically I offer patients organic calf liver extract, that is if they don't care for the taste or smell of home cooked liver. In the case of liver we get our iron by absorbing the iron containing hemoglobin molecule. In this manner up to 30% or 10 to 30 times more of the iron is absorbed.

Some health food stores offer chelated minerals, since in this form the bound minerals can be absorbed more efficiently. In the case of Cal Mag IP6, the calcium and magnesium are bound to the IP6 molecule. The IP6 molecule can be thought of as providing the "ride in". **For minerals, it's truly a case of not so much what you consume, rather what you absorb.**

For every 1000 milligrams of Inositol + Cal Mag IP6 there are approximately 152 milligrams of calcium and 47 milligrams of magnesium. With Cal Mag IP6 the mineral content can vary by 10 to 15% due to the extraction process from rice bran. The milligram numbers above represent 4 calcium and 2 magnesium atoms attached to each molecule of IP6. Some of the molecules may have 5 calcium and only 1 magnesium or they may have 3 of each etc, but overall the average is reported to be 4 calcium and 2 magnesium. I have not seen estimates as to what percentage of the minerals are absorbed. However, as most of the IP6 is absorbed if taken in supplement form, I would then estimate that a high percentage of the calcium and magnesium is carried in with the IP6 and therefore absorbed as well. This being the case, I would speculate that when the word gets out that **Inositol + Cal Mag IP6 will become one of the most sought after calcium supplements.**

When I was a naturopathic student, a couple of my professors were great fans of magnesium, since research indicated that a deficiency was implicated in several health conditions. At the time as I recall, magnesium was considered one of the most, if not the most common mineral deficiency in America, with the average American consuming less than the recommended daily allowance or RDA.

Magnesium has several key functions, but in terms of bone density, it helps to ensure that proper calcium crystal structure occurs in the bones. Even without a state of osteoporosis, bones can still be weak and prone to fracture when the underlying matrix has not been constructed properly.

When Inositol + Cal Mag IP6 first became available a few years ago, the main hesitation on the part of consumers was in regards to the potential of the molecule to deplete calcium and magnesium, since IP6 is a natural chelating agent (see the Safety chapter). This was simply a case of misinformation, as many people did not realize that the right form of IP6 would in fact be a very significant and most importantly, a highly absorbable source for these minerals.

Depression & Mood Disorders

I believe a terrible oversight is taking place in the treatment of depression.

I don't get patients bouncing into my office full of energy complaining of depression. What's wrong with this picture? Energy and depression are almost mutually exclusive, polar opposites, rarely occurring together. In my opinion, plain and simple, depression is usually a symptom derived from a lack of energy. Anything that depletes our energy or vital force can lead to depression.

Somehow, unlike Chinese medicine where the mind and body are considered as one, we have come to believe in western medicine that the mind and body are separate. They're not! Pharmaceutical companies have led us to believe in the "chemical imbalance" theory. Depression was never due to a lack of Prozac and never will be. Rarely have I seen a joyous person on selective serotonin reuptake inhibitors (The class of drugs called SSRIs that are typically used to treat depression). These patients merely aren't as sad as they were before, but they're certainly not happy.

The SSRIs are good "bandaids" as they allow people to function, yet these people rarely if ever get the most out of life. WHY? It's simple; they don't treat the cause of depression.

The cause can be anything that depletes one's energy such as poor sleep, inadequate nutrition, worry, lack of exercise, stress, poor relationships, illness, anxiety etc. Please keep in mind that there is depression due to illness or the loss of a loved one etc. That's not the

type of depression I am speaking of here. I am talking about the great many people that are simply not happy and don't really know why. It seems that this type of depression is almost reaching epidemic proportions, or is it? I think there is an epidemic occurring, but it's largely one of fatigue instead.

Even by definition (according to the DSM IV), depression in western medicine is determined by a collection of symptoms. Without spending a page or two talking about the definition of depression, suffice to say that a diagnosis of clinical depression "technically" requires 5 of the following 9 symptoms: depressed mood, decreased interest in pleasurable activities, weight gain or loss, insomnia or hypersomnia, agitation or restlessness, fatigue or lack of energy, inappropriate guilt, inability to think or make decisions and thoughts of death or suicide. The bottom line is that depression is often a symptom of an imbalance and not itself a disease. The real question is what is out of balance causing the symptom.

Fatigue or lack of energy is even one of the symptoms listed. However, I believe it is more than just one of the symptoms, but is the one symptom that naturally leads to depression. We need energy to be happy. Without energy it's tough to wear a smile.

Years ago I helped with the introduction of St. John's Wort into Canada by lecturing and writing etc. St. John's Wort is a plant that was and is extensively used in Europe to treat depression. At one point I saw statistics indicating that St. John's Wort was 8 times as popular as Prozac in Germany.

Perhaps the most interesting thing about St. John's Wort is that some research has indicated that it may not even reach the brain. The brain is protected by a special membrane that is very selective (blood brain barrier) and only allows certain molecules to cross over from the blood stream. If St. John's Wort never reaches the brain cells or neurons, then it surely begs the question; how or why does it even work for mild to moderate depression?

St. John's Wort has been shown to normalize the levels of a hormone called cortisol that can be elevated for a number of reasons, including physical or emotional stress. When cortisol is elevated it can interfere with sleep patterns resulting in insomnia. People taking St. John's Wort often report sleeping better. Better sleep usually means more energy and that in turn usually means a better mood or less depression.

In a similar manner, men using saw palmetto, which is an herb that is commonly used for frequent nighttime urination due to an enlarged prostate, also often report an improved mood. Why? The same reason as St. John's Wort: the men sleep better not having to wake to urinate and therefore their energy improves lifting their spirits.

B vitamins can be effective for mild depression. Why? I believe because of their positive effects on energy metabolism.

Another evidence-based natural medicine used for depression is SAM-E (S-Adenosyl methionine), which is a nutrient with some B vitamin-like characteristics. SAM-E is considered more potent than folic acid or other B vitamins when it comes to normalizing homocysteine levels, which is considered important for both atherosclerosis and osteoporosis prevention. Again I feel the value of SAM-E for depression may be due to the B vitamin-like effects when it comes to boosting energy levels.

Anxiety and depression are often confused. It takes more energy to be anxious than it does to be calm. Anxiety can be very draining physically. After a period of high stress or anxiety, patients often report feeling flat or drained. Depression is often the result shortly afterwards.

I am not an expert when it comes to manic depression, but in my experience high stress or anxiety often precedes the manic phase. The irrational thinking and actions taken during the manic phase seem to often be an inappropriate stress response. After a short manic phase (relative to the length of the depressive phase) the depression is usually intensified. Again the depletion of energy due to stress and anxiety ultimately leads to depression.

Child birth is perhaps the most obvious set up for depression. What can be more depleting physically than the creation of life, not to mention the countless sleepless nights. Clinically for most of my pregnant patients I recommend encapsulated liver extracts before and after their child is born. (see www.enzy.com aqueous liver extract) In addition to a wonderful source of iron (non constipating form), liver is also one of the best naturally occurring sources of B vitamins. Again I'm using an "energy tonic" for both the prevention and treatment of post partum depression.

Have I made my point? Okay, so what's Inositol + Cal Mag IP_6 got to do with energy? In short, a lot. Our bodies derive glucose from our food, which is a basic sugar that much of our existence depends on. Then the glucose is used to produce ATP (Adenosine TriPhosphate). ATP is a molecule with three phosphate groups. ATP has been called the "energy currency" in our bodies. When energy is required, one of the three phosphate groups on ATP is removed and it then forms the double phosphate ADP (Adenosine DiPhosphate). When this happens energy is released, thus enabling our life processes to take place. Cal-Mag IP_6 with 6 phosphates [as opposed to only 3 for ATP] could certainly be a better or stronger "energy currency" and just like ATP, in the body IP_6 sheds one or more of its phosphates to convert into IP_5, $_{4, 3, 2, 1}$ and finally inositol. These liberated phosphates could certainly enter into the local "energy currency" ADP-ATP cycle…..there is just more money for our body to have and spend!

In nature, a wonderful demonstration of a similar process takes place in the ocean. I often visit the outer Pacific coast of Vancouver Island. On a moonlit night you can move an object through the water making beautiful fluorescent designs. In this region there is a tremendous amount of phosphorus contained in the small sea life. When they are disturbed by motion, they then give off light. You can literally use a stick and "write" in the water. As light is a form of energy, this is similar to what's taking place in our bodies, which is the release of energy by the phosphorus containing molecule.

It turns out that glucose is the molecule from which inositol is made. This process takes place within the kidneys with approximately 4 grams per day being produced. This process also takes place within our cells as some of our glucose is converted to inositol. With diabetes there is often a problem of getting the glucose into the cell, which can then lead to a deficiency of inositol in diabetics. The diabetes chapter mentions how some of the disorders associated with this condition can be treated with simple inositol supplementation. As inositol is derived from glucose and IP_6 contains phosphorus and inositol, it is easy to see that energy metabolism is affected by this molecule.

Inositol at doses of 50 grams (50,000 milligrams) daily was taken orally and demonstrated no toxicity according to Michael Lesser M.D. He also found that inositol had a mild anti-anxiety effect similar to that of mild tranquillizers, but without the side effects. The inositol level in a variety of neuropsychiatric conditions has been found to be below normal. Clinical studies have shown inositol to be useful in a number of mental health conditions. Inositol has been found to reverse induced seizures in test animals. It can help to induce sleep. Clinical trials with inositol have found it useful for clinical depression, panic disorder and obsessive-compulsive disorder at doses ranging from 12 to 18 grams daily.

As both IP_6 and inositol are naturally occurring compounds there is really little financial incentive for pharmaceutical companies to invest in research. If they found it to be effective, how then would they profit? The other stumbling block when treating depression is the mindset that almost insists on altering brain chemistry. This strategy ignores the root cause, which in many cases is simply a lack of energy. Without question more research is needed in this area. Presently more dramatic diseases such as cancer will likely attract more attention and therefore research dollars. In the research to date however, no toxicity has been found and positive outcomes have been the result. My expectation is that clinical studies will validate and further expand on this early research. In terms of how much benefit can be expected, I would speculate that whenever stress and or fatigue are major contributing factors, then the impact of Inositol + Cal Mag IP_6 will be greater. If a patient is challenged by depression, panic attacks or an obsessive-compulsive disorder then this supplement is certainly worth considering. Inositol + Cal Mag IP_6 compliments other medications, there is little if any risk at reason-

able dosages and it would very likely offer some degree of relief.

Diabetes

Any program designed for general preventive medicine must and I mean must, address diabetes. In the United States approximately 17 million or 6% of the population are diabetic and of these, 400,000 will die each year. With stats like these, it's easy to see why diabetes is one of our leading causes of premature death. The vast majority, approximately 90% of diabetics suffer from Type II or adult onset diabetes, which in most cases is preventable with exercise, diet and weight management. One of our biggest killers is largely preventable and what are we doing about it? Sadly, not nearly enough. Traditionally the onset of Type II diabetes typically occurs after age 45. However, today the incidence of Type II diabetes is growing rapidly in our young people. The bottom line: we're losing this battle too!

How can Inositol + Cal Mag IP_6 help in the struggle with diabetes? To start, diabetes is a disease in which the Beta cells of the pancreas produce less or in some cases almost no insulin. Insulin is a hormone that enables glucose (sugar) to enter our cells so that it can be used to produce and store energy in the form of ATP, which is a "battery like" triple phosphate molecule. When glucose is unable to enter the cell, the result is high blood sugar levels or what we call diabetes. Just over a year ago (Dec 2002), C. J. Barker and his associates published a paper in the American Journal of Physiology-Endocrinology and Metabolism [See www.ajpendo.org] The paper was a review of the role of phosphorylated inositols (IP_1 to IP_6) in relation to insulin secretion. Quoting the authors: "Inputs from glucose and cell surface receptors act together to initiate the beta cell stimulus-response coupling that ultimately leads to the release of insulin. Phosphorylated inositol compounds have recently emerged

as key players at all levels of the stimulus-secretion coupling process". The authors go on to mention that IP_6 in particular, is now known to have new roles in this process. In plain English, this means that phosphorylated inositols, particularly IP_6 are needed for insulin secretion. Be careful, as this doesn't mean that IP_6 leads to insulin secretion, rather that IP_6 at the very least is necessary for the process to take place.

There are a number of serious complications common to diabetics such as:

1- clogged arteries that can lead to high blood pressure, heart attack and stroke
2- damage of the retina and an increased incidence of cataracts. Diabetes is the leading cause of blindness in persons 20 to 74.
3- kidney damage (nephropathy), 40% of kidney failure is caused by diabetes
4- neuropathy which can effect sensation causing numbness and or burning pain
5- high risk pregnancies leading to more miscarriages
6- limited or weakened immune response leading to frequent or serious infections

Inositol metabolism is directly affected in those with diabetes. Inositol is made from glucose both by the kidneys as well as within the cells. For those with diabetes, getting glucose into the cells is the challenge due to a lack of insulin. A shortage of glucose entering the cells can ultimately lead to an inositol deficiency within the cells.

When diabetes is induced in animals, the level of inositol in peripheral nerves has been shown to be lower. This can lead to movement and sensory deficits as the nerve impulses travel slower than normal. Insulin normalizes both the inositol levels as well as the speed of nerve conduction. Inositol supplementation too has proved beneficial in restoring motor nerve velocity. Inositol has been tested clinically for peripheral neuropathy. Trials have used between half a gram twice daily and up to 3 grams per day. The results have indicated that inositol may benefit and therefore be useful in the treatment and prevention of nerve problems associated with diabetes. As

opposed to glucose which needs insulin to enter into the cell, inositol and IP_6 do not; they enter the cells very quickly.

As a potent antioxidant there is good reason to believe that this supplement will potentially inhibit cataract formation.

Diabetics are often more prone to infection as a result of an impaired defense. Please see the immune system chapter for ways in which this supplement supports our immune response.

Diabetics typically have a shortened life span, due primarily to the cardiovascular consequences of having elevated blood sugar levels. Both large and small vessels can be affected. Blockage of the large vessels can result in strokes or heart attacks. Impairment of the microcirculation can cause retinopathy or damage to the retina, which can eventually lead to blindness. Damage to the microcirculation can cause damage to the kidneys (nephropathy). This can impair detoxification and filtering processes and can eventually lead to kidney failure requiring dialysis. Another problem common to diabetics is impotence, as a result of impaired peripheral blood flow. Much of my consultation with a diabetic patient is educational, explaining how to prevent the cardiovascular problems associated with diabetes.

A targeted comprehensive approach is essential. The difficulty is that patients have to be continually re-motivated, as cardiovascular disease development is very slow, taking years and at the same time it is insidious, not causing any symptoms until well progressed. It's for good reason that it's called the silent killer. Inositol + Cal Mag IP_6 offers several mechanisms with which to support the cardiovascular health of diabetic patients (see the Cardiovascular Disease chapter). In addition to this supplement, with diabetics I often recommend a variety of supplements and life style changes due to the severity of the potential pathologies. The good news is that the complications of diabetes can be prevented or at least delayed.

Diabetes can cause congenital defects in the fetus leading to miscarriage. The incidence of an abnormality in the embryo (embryopathy) in diabetic mothers is 4 to 5 times higher than average. The reason

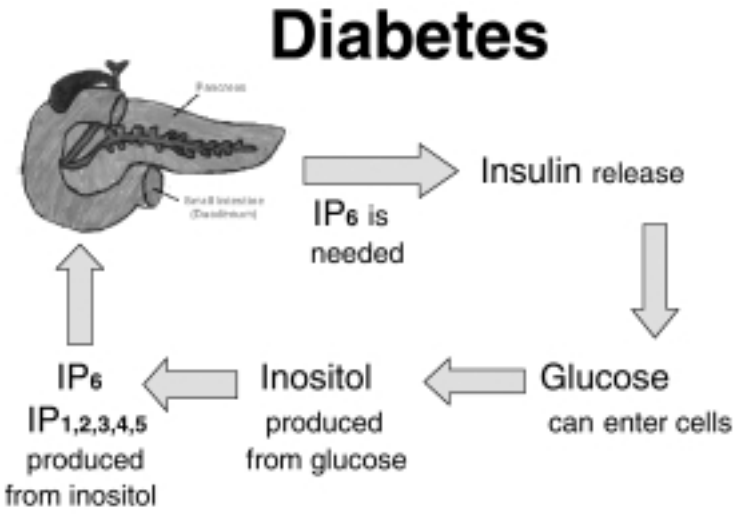
for this was found by several researchers to be excessive oxidation by oxygen free radicals and changes in the inositol level in the embryo. There is experimental evidence suggesting that as glucose levels in the embryo increase that the inositol levels fall. Inositol supplementation has been found to decrease malformation rates, while normalizing inositol levels. Although IP_6, which is a very potent antioxidant, has not yet been tested, other antioxidants and inositol have been and according to Reese, and Eriksson (1996) "offer significant promise for the future in possibly serving as a pharmacological prophylaxis against diabetic embryopathy". Dr. Reese and his associates were able to show that inositol also decreased the incidence of neural tube defects. The B vitamin folic acid, is today prescribed for this very purpose. Hailed as a major medical breakthrough in the 1990's, few realize that folic acid was in fact proven to prevent neural tube defects 4 decades earlier. Hopefully, the awareness of inositol's benefits won't have to wait 4 decades.

A sociology professor in Maryland provided some interesting anecdotes when I spoke with him regarding diabetes. I was given his name by Dr. Shamsuddin, who said the professor had applied for a study grant to investigate the effects of Inositol + Cal Mag IP_6 on diabetics, based on his own blood sugar counts. Himself a diabetic, the professor has been using the supplement for a number of years and found that his blood sugar levels were much more stable and somewhat lower. He applied for research grants to study the benefit of this very simple and inexpensive supplement on the under-served urban population in the City of Baltimore. Unfortunately his application was not approved (most aren't due to a scarcity of research dollars), nevertheless he is still a strong proponent of the supplement recommending it to several diabetics in his department.

He reported several health improvements in his colleagues and himself. I was most fascinated with the perspectives he provided of growing up in a rural village in Bangladesh, as these are insights that are generally unavailable to me living in the western world. As a sociologist he was intrigued by the fact that the poorer people seemed to enjoy more vibrant health and feels it was due to more than just the variance in stress levels between the two groups. The

main dietary distinction between the haves and have-nots appeared to be the type of rice eaten, as only those with more money could afford the polished or white rice. A well-known benefit of rice polishing (rice bran) was the improved health of the villager's cows. Cows are an important part of rural village life. For centuries only the wealthier were able to feed their cows the rice polishing. The cows that were fed the rice byproduct lived longer, were generally healthier and produced more milk. I found the professor's tales ironic, as only the cows of the affluent enjoyed better health, but not the affluent themselves.

Where does one start when evaluating the relationship between blood sugar and this supplement? The two are inseparably linked in every which way. Glucose, which is our prime source of energy, is the mother of inositol, which is in turn the mother of IP_6. The phosphorylated inositols (IP_1 to IP_6), especially IP_6 are necessary for insulin secretion. Insulin is necessary for glucose transport into the cell. And so the cycle repeats on and on endlessly. Add to this, the fact that glucose is converted to energy in the form of ATP, which requires phosphate groups of which IP_6 provides six. What eventual fruit this relationship will bear only time will tell. I'm very interested to find out whether Inositol + Cal Mag IP_6 can aid in the prevention of diabetes. However, with what we know now, it would seem wise to support diabetic protocols with the supplement, not only to normalize inositol levels, but to also take advantage of the molecule's potential to limit the cardiovascular side affects of diabetes. And so the cycle repeats on and on endlessly. (see the diagram on the next page)



9.1

Cardiovascular Disease

Cardiovascular disease (CVD) may not be as feared as cancer, however it is still our most prolific killer. Most Americans don't realize it, but more U.S. citizens die every year from CVD, than have died in all the wars America has been involved in, including World Wars I & II as well as Vietnam, and now Iraq.

IP_6 has primarily been researched for its anti-cancer effects. However, some of the mechanisms that have come to light also offer the potential to prevent heart attacks and strokes.

Our emphasis on CVD prevention has traditionally focused on blood pressure and cholesterol level management. Recently the statin class of drugs, which are by far the most commonly employed lipid lowering agents, have come under fire. Why? Clearly, elevated cholesterol levels are a risk factor that can lead to blocked arteries, clearly the statins such as Lipitor or Pravachol lower cholesterol levels, but whether the statins prevent heart attacks and strokes when used for primary prevention is not at all clear.

The Therapeutics Initiative program at the University of British Columbia is comprised of specialists who are experts in the particular therapeutic area. They "study the studies." Therapeutics Initiatives is a member of the International Society of Drug Bulletins who are financially and intellectually independent of the pharmaceutical industry [see http://www.ti.ubc.ca/pages/letter48.htm and http://www.isdbweb.org/]. The researchers reviewed data from 5 clinical trials, which included almost 40,000 patients and showed a less than 2% decrease in heart attacks and

strokes over a three to five year period and an almost equivalent increase in other serious adverse effects. The conclusion: "Therefore, statins **have not** been shown to provide an overall health benefit in primary prevention trials". Primary prevention in this case refers to patients who have not yet had a heart attack or stroke and have a risk factor such as elevated cholesterol.

This report was controversial and especially alarming, considering that $15 billion dollars are spent annually on statin drugs. Not millions, but billions! In Canada the estimate is $1.4 billion alone. At a time when health budgets are being squeezed everywhere, wouldn't one expect that such an enormous treatment expenditure first need be proven to work?

This just goes to show how powerful pharmaceutical lobbyists really are. In reality we may be spending billions on medicines that are utterly useless. Can you imagine how much fiber 15 billion dollars would buy? In addition to other potential benefits such as decreased constipation and lowered cholesterol levels, I'd be willing to bet that heart attacks and strokes would fall by more than 1 or 2%.

There are several evidence based natural medicines such as Policosanol (sugarcane extract see www.policosanol.com), gugulipid (myrrh), flush free niacin, garlic and red yeast rice etc that effectively lower cholesterol. In fact, the statins are derived from red yeast rice, which is a traditionally used Chinese medicine for "stagnant blood". Drug companies have been able to alter and therefore patent the molecules that occur naturally in red yeast rice. These new molecules (statins) aren't necessarily more effective, only far more expensive. Shouldn't governments at least investigate red yeast rice itself before spending billions on the patented versions? Who knows, maybe it's safer and at the very least would only be a fraction of the cost. In terms of safety, the statin Baycol was recently discontinued after several patients died.

Even IP6 has been shown to lower cholesterol and triglyceride levels in animal studies performed at the Linus Pauling Institute of Science and Medicine. However, I truly feel that there are better ways to prevent heart attacks and strokes than by simply lowering cholesterol levels. Some research suggests that risk is dependant not so much on having arterial plaque, but rather on how stable the plaque actually is. As long as blood can pass through an artery and a piece of plaque doesn't dislodge, then generally a patient is at less risk. A high degree of systemic inflammation is strongly correlated with a low degree of plaque stability. In other words, if we can decrease inflammation then we can lessen the chance of a piece of plaque breaking off and plugging an artery causing a heart attack or stroke. There are several dietary, drug and supplemental ways to reduce inflammation. IP6 has also been shown to reduce inflammation in a number of research models unrelated to heart disease.

I believe that Inositol + Cal Mag IP6's ability to inhibit platelet aggregation or blood "stickiness" is its most important characteristic when it comes to preventing serious cardiovascular events, especially in those with preexisting plaque formation. The use of aspirin is becoming common place for this very reason. Many people question the use of alcohol consumption. There have been several senior patients who, when first coming to the clinic, feared that I would recommend discontinuing their daily cocktail. Usually I don't, as most studies indicate that moderate alcohol consumption increases longevity. Why? I believe it's because alcohol inhibits platelet aggregation, thereby preventing heart attacks and strokes. There are many nutritional, drug and supplement options that can do the same, of which Inositol + Cal Mag IP6 is one.

As a formidable antioxidant, IP6 has the potential to arrest the initiation of plaque formation before it begins. The endothelium or inner lining of our blood vessels normally has to be injured or slightly disrupted for the initiation of plaque formation to commence. If the lining is healthy, there is less chance of cholesterol attaching and penetrating the vessel wall. Antioxidants are thought to be one of the prime forms of protection for the endothelium. Grapeseed extract is a very popular antioxidant supplement, that's used for this purpose. The reasoning behind the "French Paradox" has contributed to the success of grapeseed. The French consume a very rich diet with a lot of cheese, yet they have far less heart disease than would be expected. The antioxidants found in the pigment of red wine, are believed

to be responsible for the paradox. I believe that the alcohol content of wine may also be swaying the statistics in their favor.

As an antioxidant, IP6 has been researched as an agent to reduce the damage that occurs to heart muscle after a blood supply is reestablished (reperfusion injury) following a heart attack. Damage to heart muscle occurs both when the blood supply is cut off (due to a clot or constriction of vessels) as well as when the blood supply resumes. It seems counter-intuitive that the resumption of blood flow would cause damage, however because of potent oxidants occurring in blood, the heart muscle or myocardium is vulnerable to oxidation following an interruption of blood supply. Researchers first administered IP6, then induced heart attacks and then allowed the blood supply to the hearts of the test animals to be reestablished. There was a very significant protective effect found in IP6 treated animals in comparison to the control animals, which did not receive IP6. Dr. Parinam S. Rao and his fellow researchers from the Long Island Jewish Medical Center and Albert Einstein College of Medicine in New York, and the University of Connecticut College of Medicine in Farmington concluded: " These results suggest…..Phytic Acid [IP6], a natural antioxidant, may provide a promising tool for protecting an ischemic heart from reperfusion injury,".

Years ago I was at a medical conference and was very intrigued by one of the speakers who presented reasoning as to why women live longer on average than men. Prior to this, most were led to believe that it was due to the cardiovascular protective effect of estrogen. This seemed a reasonable hypothesis as women have fewer heart attacks before age 50 when estrogen levels are high. After menopause as estrogen levels decline the cardiovascular risk to women increases and the gap between male and female risk narrows. The lecturer made me really think when he said research had indicated that men who gave blood regularly, lived as long as women. He never mentioned it, but at the time I kept thinking this guy should be doing blood bank commercials: "Give Blood … Live Longer". It may in fact be the lower iron levels due to menstruation that is protecting women from excess oxidation and therefore damage to blood vessel walls.

IP6 is known to chelate (bind) iron and remove it from circulation. If the hypothesis of keeping iron levels moderate to prevent atherosclerosis turns out to be correct, then this is yet another mechanism by which IP6 could prevent CVD.

As chelators, the breakdown products of IP6 (the lower IPs) have been shown to lessen the calcification of arteries in animal studies. Until Dr. Dean Ornish published results showing that the levels of arterial plaque could in fact be reduced by a very strict adherence to a healthful diet and exercise program, most physicians didn't believe that unclogging of arteries was even possible without bypass surgery. If studies show arterial calcification reversal occurs in people using IP6, then you can bet that this will also be one the most sought after cardiovascular agents. You can also expect drug companies to develop synthetic clones so the molecules can be patented. You should also expect to no longer be paying for a concentrate from rice bran, instead for a new class of cardiovascular "life saving" drugs. If you're wondering what the new costs will be, just look at statins as an example. It's easy to speculate that this new class of drug would even be more expensive than the statins, as these new agents would be used to reverse existing plaque deposits. As IP6 can also bind aluminum, which is implicated in Alzheimer's disease, I am also hoping that the chelating effect of IP6 will prove to be beneficial in the prevention of Alzheimer's as well.

The only concern that seems to arise with IP6 is the ability of it to bind minerals (see the safety chapter). Studies looking to uncover mineral imbalances in the blood and bones of animals fed high doses of IP6 haven't demonstrated any abnormalities. In people as well as animals, elevated cholesterol levels can be accompanied by too much zinc relative to copper. In studies in which animals were fed high cholesterol diets, their zinc to copper ratios were restored to normal when consuming IP6. On the other hand, if the same animals were fed healthy diets, the zinc to copper ratio did not change and remained normal even with high levels of IP6 in their diet. In addition, Cal Mag IP6 is a great source of calcium and magnesium. Calcium and magnesium have several functions, but in terms of cardiovascular health, both minerals help to maintain healthy blood pressure levels.

The concern of mineral deficiency should never become a reality since we have easy access to multivitamins with plenty of minerals. With intravenous EDTA chelation therapy, a multivitamin is simply taken away from the treatments, to insure a deficiency doesn't result. IP_6 offers several advantages over EDTA chelation therapy. First is safety, Cal Mag IP_6 can be used and therefore provide benefit on a continued basis. Deposition of calcium and plaque is an ongoing process and is probably better addressed by a consistent therapy. Second is cost. EDTA typically costs $4000 to $6000 for a series usually consisting of 30 to 40 treatments. This supplement on the other hand is approximately $20 to $30 per month unless higher dosages are used as with cancer patients. Third is the convenience of a supplement in contrast to EDTA chelation, which requires being hooked up intravenously for periods of 2 to 3 hours at a time.

Neither EDTA nor IP_6 has been clearly proven to open clogged arteries in people. The logic for IP_6 as a chelating agent is perhaps best demonstrated by its effectiveness in treating kidney stones. Very recently (May 2004) Dr. Grases and his colleagues published the results of a study demonstrating that IP_6 prevented the deposition of calcium in soft tissue as well, presumably by the same mechanism. I personally don't provide EDTA chelation in my practice, but as a student I did a practicum at the Dr. Ray Evers clinic in Mexico. He was a medical pioneer treating thousands of patients since the 1950's with chelation. From my experience at Dr. Evers clinic and from discussions with my current colleagues, the sense I have is that EDTA chelation makes a major difference in approximately one third of patients, one third experience minor improvement and one third unfortunately don't seem to benefit, at least symptomatically.

Stroke and heart attack prevention requires a multifaceted approach. Diet and lifestyle are central to keeping our arteries clear. Simplistic as it may sound, I believe that the heart is significantly affected by emotion and that healthy loving relationships are an important component of heart health. Fortunately many medical authorities now consider much of our current CVD epidemic to be preventable. This is an empowering perspective. Yet fewer and fewer persons are taking advantage of this opportunity to determine their own fate. Childhood obesity is raging out of control. If preteens with high metabolisms are overweight, what are they going to do in their 40's when metabolic rates typically slow down? The clinical cardiovascular research on this supplement is minimal, however all the right mechanisms of action appear to be there. In mostly animal studies, this supplement has demonstrated that it can inhibit inflammation, inhibit platelet aggregation, regulate blood pressure and cholesterol levels, is a potent antioxidant, binds iron and has been shown to even reverse plaque formation in arteries. I expect in time that Inositol + Cal Mag IP_6 will come to be known and employed as a safe, effective therapy in the prevention of CVD.

Kidney Stones

Patients have told me that passing a kidney stone was more painful than delivering their children. Having heard patients describe their ordeal with kidney stones makes me want to absolutely avoid the experience if at all possible.

From 1% to 5% of the population form renal calculi (stones), of which 80% to 95% of those are composed of calcium oxalate or calcium phosphate. Fortunately many do not experience symptoms, or pass small sand-like sediment or stones with no complications. Unfortunately, for those that do manage to get a stone lodged in the ureter, which is the tube running to the bladder from the kidney, they often have a tale of severe pain to tell.

In 1958 Dr. Philip H. Henneman and his associates at Harvard Medical School and Massachusetts General Hospital in Boston published the clinical results of 35 men using IP_6 in *The New England Journal of Medicine*. The patients had normal blood levels of calcium, but increased levels in their urine (idiopathic hypercalciuria), which is the main risk factor for kidney stones. The men took 8.8 grams of sodium IP_6 orally in divided doses. The patient's urine calcium levels returned to normal. 10 of the patients took the IP_6 for an extended period (on average 24 months) and only 2 of these 10 developed a kidney stone. The result was that IP_6 normalized the hypercalciuria and significantly lessened stone growth and recurrence. The treatment of the day was a low calcium diet (avoidance of dairy) and increased fluid intake, which offered limited success. This begs the question: why if a safe and much more effective treatment was revealed, was it not followed up and investigated further?

The only answer I can come up with is that being a natural product drug companies might shy away due to lack of patent protection.

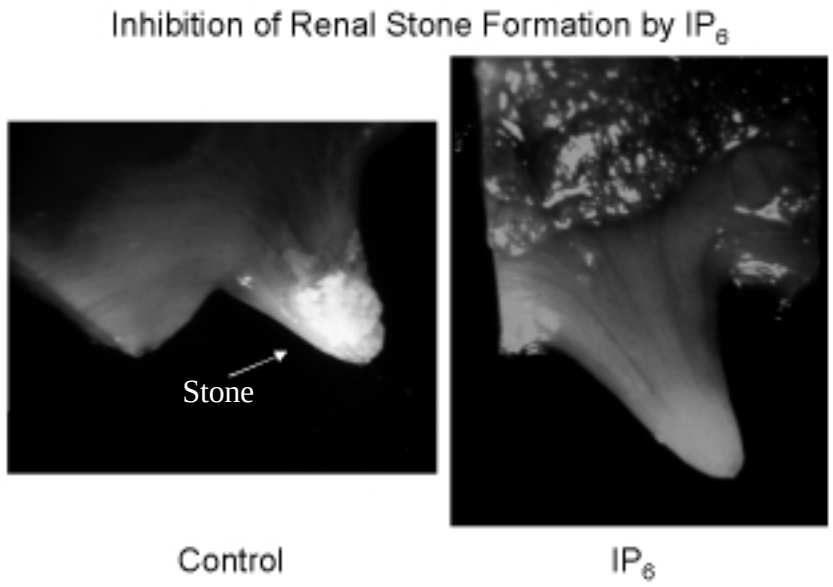
Four decades later, Professor F. Grases presented research at the Kyoto Japan "First International Symposium on Disease Prevention by IP_6 and Other Components of Rice". Professor Grases showed a significant inhibition of calcium oxalate crystallization, which is a key event required in kidney stone formation with IP_6 in an in vitro study. In a clinical study with 74 patients (who were calcium oxalate stone formers) he showed that the risk of calcium stone formation was reduced in contrast to the control patients within 2 weeks after being treated with 120 mg of Cal-Mag IP_6 (LitStop™) daily. As you can see the dose of 120 mg is a much lower than used in the Harvard study performed decades earlier.

Very recently (April 2004), Dr. Curhan and his associates at Harvard published results from the Nurses Health Study II. The women filled out detailed food frequency questionnaires in 1991 and 1995. The 96,245 women had no prior history of kidney stones. The researchers prospectively examined during an 8 year period the association between dietary factors and the risk of symptomatic kidney stones. There were two main conclusions from the study, both of which were very interesting. First, "A higher intake of dietary calcium decreases the risk of kidney stone formation in younger women, but supplemental calcium is not associated with risk". This finding completely contradicts the strategy of limiting calcium intake as has often been suggested. Further, since Cal-Mag IP_6 provides a substantial amount of calcium, perhaps it is also benefitting kidney stone formation in this manner. Secondly, and highly relevant to our discussion was this concluding statement: "Finally, dietary phytate [IP_6] may be a new, important, and safe addition to our options for stone prevention." Considering the enormous size of the study group, this becomes a highly significant finding.

Kidney stone incidence has been rising since the late 19th century in Europe and North America as well as in Japan since World War II. The rise in kidney stone incidence correlates closely with dietary change towards a more refined diet, which typically offers less IP_6.

Hospitalization statistics of South African blacks provides more convincing evidence as to the value of IP_6 containing foods for the prevention of kidney stones. From 1971 to 1979 Dr. Monte Modlin of the Medical School of Cape Town reported that 1 of every 510 white patients admitted to the school's teaching hospital were for kidney stones. In contrast only 1 of 44,298 black admissions was for kidney stones. That's almost a 90 fold difference! In Cape Town in 1970, 5.1 million blacks and 4.5 million whites lived in the urban areas. For blacks moving from the rural to urban areas it generally results in more meat consumption. However, the diet is still based on daily maize or corn consumption of about 680 grams. As corn may contain up to 6% IP_6, it works out to a whopping 40.8 grams of IP_6 daily.

The proposed mechanism for kidney stone prevention using IP_6 is called chelation. The word chelation comes from the Latin word chele, which means a crab's claws. Thus chelation refers to using medicinal agents that have the potential to grasp or bind with other molecules. Approximately 1 to 3% of IP_6 leaves the body via the urine. The IP_6 exiting via the urine is able to bind and remove calcium atoms that make up or are part of kidney stones. Bound together, the IP_6 and excess calcium are then both eliminated from the body. A kidney stone contains millions of atoms of calcium. This is like removing a single grain of sand, after single grain of sand, and so on and so on from a sandbox. Eventually the sandbox will be emptied as will the kidney stone be slowly dissolved. Thus IP_6 provides a safe and effective treatment. It's purely a case of having enough IP_6 in the urine to do the job. How much is the question, as both trials above were highly successful (as was the prospective study), despite a wide range of dosage. The following pictures show how the kidney stone at the tip of the kidney tissue of the IP_6 treated animal is no longer present in contrast to the control animal in which a stone is still present.



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If you've had a kidney stone, chances are you'll have another. As such, a preventive strategy is usually called for. Current therapy often includes an increased water intake, often combined with a diuretic. Inositol + Cal Mag IP6 provides a whole new and safe approach. If you're fortunate enough to have never had an episode, this supplement is likely your best insurance aside from eating a simple, healthful diet. For myself, never having had a kidney stone, I simply think of this stone preventive aspect of Inositol + Cal Mag IP6 as yet another of its multiple benefits.

Immune Support

Our immune system can be likened to an orchestra, with the various components knowing when to play a supportive role and when to lead, but all the while working together. We have several types of white blood or immune cells that work continuously, interacting to support each other and relaying information as to impending danger. When one type of white blood cell is unable to defuse a situation, there are usually others there to help out.

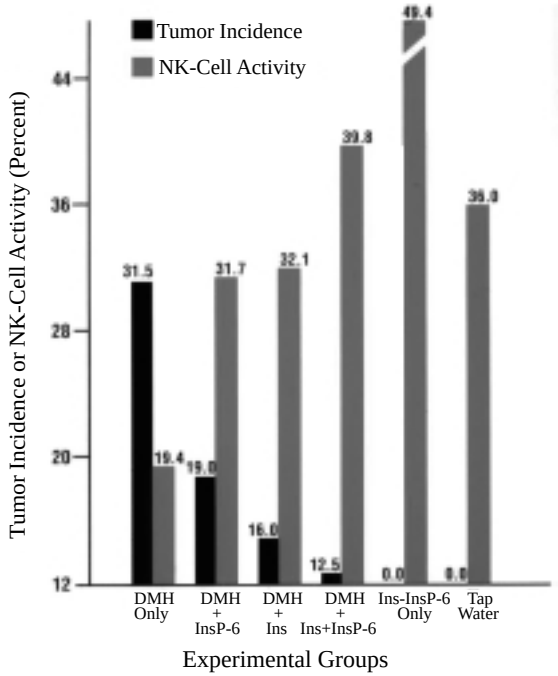
We are constantly being challenged by viruses, bacteria, fungus, allergens and cancer cells etc. For example, it has been estimated that on average we produce five hundred to a thousand cancer cells a day, yet most of the time we don't get cancer. Why? Our immune system recognizes these cells as a potential threat and destroys them. The vast majority of the time the immune system is so efficient that we don't even realize that our health is at risk. Usually it's only when we get a cold or a flu that we realize a battle is on.

A number of things can impair our immune response. Excess stress of all types can wreak havoc with our defenses. Poor lifestyle, such as a lot of late nights or irregular eating habits can also lessen our immunity. How many times do you think I've heard a patient say that they caught a cold or the flu after becoming run down? Lots! Unfortunately, I have also heard a number of cancer patients express that they felt their cancer worsened or relapsed after a period of either heavy stress or being run down as well.

Nutrition can also play a role, as evidenced by research that has shown that the weakened immune responses in a group of elderly

patients was not due to age, rather it was from a deficiency of nutrients such as vitamin E in the study group. When the elderly patients were supplemented with the deficient nutrients, their immune response increased very significantly. Certainly some things can be attributed to aging, but a weak immune system may not be one of them. At the very least, when our immune function is compromised, for whatever reason, we should be considering extra support.

It has been scientifically proven, that Inositol + Cal Mag IP6 provides substantial immune support, by augmenting the response and effectiveness of a type of lymphocyte or white blood cell called a natural killer (NK) cell. This type of white blood cell targets cancer cells. There is an inverse relationship between NK cell activity and cancer incidence. In other words, when NK activity is high the incidence of cancer is much lower and conversely, when NK cell activity is low we are at a much increased risk. See the following chart. The highest NK activity was demonstrated in the Inositol + IP6 group (Ins+InsIP6).



12.1

As mentioned earlier in the cancer chapter, exaggerated or completely false statements of supplements claiming to boost NK cell activity with the potential to cure cancer are common. I wish treating cancer was as simple as boosting NK cell activity, but unfortunately its not. Boosting NK activity is believed to be extremely important for cancer prevention and also plays a role, but is certainly not the main or only strategy that should be employed for treatment.

The NK cells in fact have a dual immune role. They also play a primary role targeting virally infected cells. Viruses are certainly one of our greatest immune challenges, as there are a countless number of them and they often mutate, thereby presenting new threats. Viruses are responsible for everything from the common cold to the flu, to hepatitis to HIV, to herpes etc. Because NK cells have a key role to play in overcoming viral infections, the supplement has value as a broad spectrum immune agent. It's often been reported to me that after taking the supplement for whatever reason, that people have far fewer colds.

Very interesting viral research was performed in Japan by Dr. Toro Otake and his colleagues, when they were able to demonstrate that IP6 protected MT-4 or thymus gland cells from the HIV or human immunodeficiency virus. In the study, the MT-4 cells suffered less damage from the HIV virus when IP6 was used.

Dr. Paul Eggleton of Oxford University demonstrated that IP6 may also help in our battles with bacteria. Our primary defense against bacteria is provided by a white blood cell called a neutrophil. Neutrophils damage and destroy bacteria by oxidizing them. Dr. Eggleton was able to prove that IP6 increased the amount of oxidizing agents within neutrophils, thereby improving their ability to protect us. It's ironic but wonderful, that on one hand IP6 is one of our strongest antioxidants, yet it boosts our bacterial immune response by increasing the oxidative abilities of neutrophils.

Viruses, bacteria and cancer present the most dire threats to our health from an immune perspective. At the risk of sounding overly enthused, I don't mind saying that this molecule continually amazes me. In addition to its other health benefits, it helps to protect us from all three of these dangerous and opportunistic enemies.

Nature's Super Antioxidant IP_6

Today many people have heard of antioxidants. Most don't really understand the term, but they generally know that they're good for them. Antioxidants have frequented media headlines, as they can play a role in the prevention of so many conditions, especially those associated with aging. In fact, in addition to a healthy lifestyle, anti-aging protocols or programs typically include antioxidants and until recently, hormones as well. Hormones enjoyed a strong popularity before the studies published over the past couple of years indicated that estrogen may lead to more cardiovascular disease and not less as previously speculated. The result, antioxidants now provide the foundation for anti-aging treatments.

So what are antioxidants and how do they protect us? To illustrate antioxidant activity, one can simply think of an apple that's been sliced in half. Normally, due to the oxidants in the air, the exposed part of the apple would turn brown quickly. However, if one were to squeeze lemon juice on the flesh of the apple immediately after slicing, the apple would take longer to turn color. In this case the lemon juice contains antioxidants, which are able to protect the apple's flesh.

To understand the concept of oxidants and antioxidants it helps to have some basic understanding of cells, atoms and electrons. Basically an oxidant is an atom or molecule that is short of an electron and attempts to acquire it from another molecule, which in the case of our bodies, often happens at our cell linings or membranes. When an oxidant successfully "steals" an electron from a molecule lining our cells, it then sets up a chain reaction. The molecule that gave up the electron to the oxidant in turn tries to get one back from

a neighboring molecule in the same cell membrane. Once initiated, this process repeats itself over and over and as a result, the cell lining can become slightly weaker or damaged. The impact of this process ultimately "ages" our cells, not allowing them to function optimally. This sounds serious, but in reality it is an ongoing natural process, with oxidants "attacking" our cells in search of an electron and at the same time antioxidants providing the electron in order to minimize the damage. Antioxidants can simply be thought of as "electron donors".

To demonstrate how significant antioxidants are to anti-aging programs, one needs only to look at the lifespan of a chimpanzee. Scientists have speculated that the reason chimps live approximately half as long as humans, despite having very similar physiology and genetics, is that the antioxidant mechanisms of a chimp are not nearly as effective, resulting in faster aging and therefore earlier death.

There are many types of oxidants requiring several different antioxidants to maintain a healthful balance. Vitamin C and E as well as zinc and selenium are perhaps our most commonly used antioxidant nutrients. There are several supporting interactions between these nutrients. This is partially why in the "Designing an Optimal Supplement Program" chapter, I recommended a high quality multivitamin. Vitamins are generally inexpensive, however other nutrients such as zinc or selenium are quite a bit more and levels are often compromised in less expensive formulas.

When we eat a healthful diet with lots of veggies and fruit we are consuming several antioxidants. A simple key to ensure that we get a broad spectrum of protection is to eat a "rainbow" diet. Often the foods with the highest concentration of antioxidants occur in the colored or highly pigmented fruits and veggies.

There are hundreds of carotenoids that function as antioxidants, with lycopene and lutein presently enjoying popularity as single supplements. The carotenoids of which beta-carotene is perhaps the best known, are derived from the "warm" colored foods: yellow, orange and red. Carotenoids are interesting in terms of cancer prevention, as they protect plants from the radiation resulting from extended

exposure to the sun's rays. In people, carotenoids function in a similar manner, patrolling and protecting our tissues.

Another group of very potent antioxidants are called flavonoids. Plants and flowers often derive their color from these substances. Flavonoids are also responsible for many of the medicinal properties of plants. Some of the most commonly used flavonoid-rich herbs include ginkgo, bilberry, green tea and grapeseed extract. A very interesting thing about many flavonoids is that they often seem to be tissue specific. For example bilberry supports the eyes primarily, gingko and grapeseed the blood vessels and milk thistle the liver. Tissue specificity is a tremendous advantage therapeutically, as it enables us to target particular areas (unlike most drugs) and thereby avoid unwanted effects.

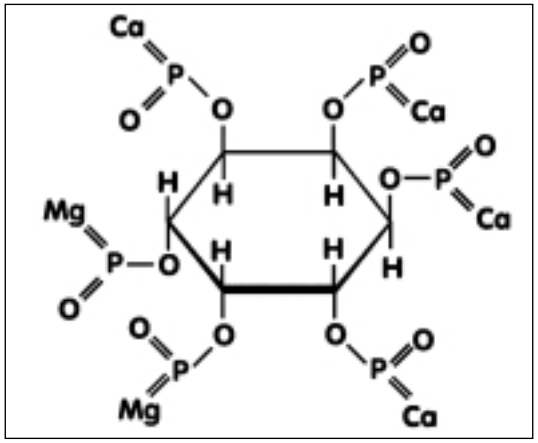
As a famed antioxidant, green tea has been extensively studied for its anti-cancer affects. The Japanese have one of the longest life expectancies and many attribute their longevity to the regular consumption of green tea. When I attended the international symposium on IP6 in Kyoto Japan, I discovered just how significant green tea is to the Japanese. Not only was green tea the main drink, but they also had cakes, cookies and ice cream etc all made with green tea.

Researchers Challa et al, published results in the journal Carcinogenesis (1997), in which they investigated the anti-cancer effects of green tea versus IP6, as well as the combination of both. The investigators wanted to know which nutrient was better able to prevent colon cancer and whether there was a synergistic effect when green tea and IP6 were used together. There results showed that green tea had a marginal effect, whereas IP6 had a much more pronounced effect and that, yes indeed there was a very strong enhanced or synergistic effect of the two together.

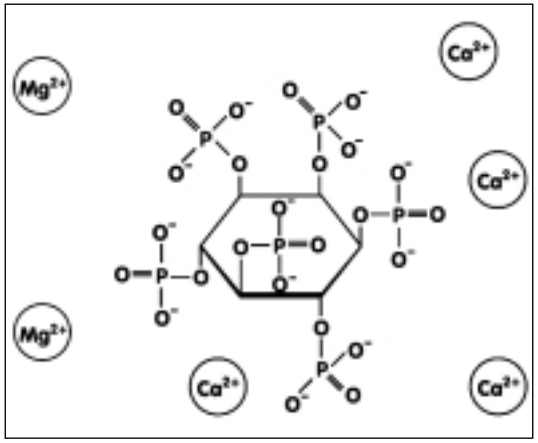
As a supplement, when we consume IP6 it's usually bound to minerals such as sodium, iron or calcium and magnesium. In the case of Cal Mag IP6, the molecule is bound to 6 of the double positively charged calcium or magnesium atoms. After absorption, the body then removes and uses the calcium and magnesium atoms. We are then left with an IP6 molecule that has 12 extra electrons that it can

give up and ultimately use to defuse oxidizing agents. This means that in many cases, each IP6 molecule **can neutralize up to a dozen oxidants.** No wonder this simple rice extract is one of our most potent antioxidants.

You can see in the first picture, how the calcium and magnesium are bound to phosphorus (P) in the IP6 molecule with a double bond. The double bond implies that two electrons are being shared. In the second picture the calcium and magnesium having been removed from the IP6 molecule can now be used by the body. Now there are twelve oxygen (O-) with an extra electron. The twelve extra electrons can now be used to neutralize various types of oxidants.



13.1



13.2

I previously mentioned that my antioxidant of choice was Inositol + Cal Mag IP6. I feel this way for two main reasons. First, IP6 is in all of our tissues and inside all of our cells. It can therefore provide both intracellular (inside the cell) and extracellular (outside the cell) systemic protection. Secondly, it is considered to be much more potent than even green tea. So basically, it's powerful and because it's needed for the normal functioning of cells, it occurs naturally everywhere we need it to be. In addition, research is now indicating that inositol also provides some antioxidant activity as well.

In a single generation the awareness and acceptance of antioxidant protection has risen from that of a seldom used medical term to that of a common everyday expression. I expect antioxidants to gain even more prominence due to their ever increasing use in anti-aging formulas. Because there are so many types of oxidizing agents, for comprehensive protection we need a broad spectrum of antioxidants. Fortunately by eating a rainbow selection of fruits and vegetables we can achieve most of our antioxidant requirements. Additionally, a quality multivitamin and Inositol + Cal Mag IP6 will insure optimal protection.

Designing an Optimal Supplement Program with Inositol + Cal Mag IP6

Confused? Most people are when selecting vitamins. Just look around in most health food stores and you will be confronted with thousands of options. Pharmacies usually offer fewer options, but one is often in a self-service situation, which can be even more perplexing. How does one determine which product to choose let alone whether it's a quality product, a safe product, an effective product? My first recommendation would most surely be to seek advice of someone professionally trained and licensed in the field of natural medicine. The key to any medicine whether it be western, naturopathic, Chinese etc is an in depth assessment and a thoughtful determination of treatment goals. What specifically are you trying to achieve? Different systems of medicine may offer different perspectives and as a result suggest different treatment options, but all systems of medicine try to identify the reason why a symptom or disease state is occurring. So many products are good for you, but are they good for YOU specifically. For example, how many people are fatigued? Vitamin manufacturers have responded with almost a countless number of energy remedies. The question is: Why are you fatigued? Is it anemia, insomnia, hypoglycemia, hypothyroidism, cancer, poor nutrition, lack of exercise, stress etc etc. With fatigue for instance, patients will sometimes literally bring in a shopping bag full of supplements that they have purchased at various health food stores or pharmacies. To the patient's credit they are really trying and are reaching out for help. Generally speaking the supplements are okay and have application for fatigue, but often do not address why that particular patient is fatigued. Usually I see sincere

attempts to help customers and not merely efforts to sell product from the various supplement stores, but in reality the consumer is not being helped or not being helped to the extent that they could be.

So what supplements should you take? This ultimately depends on your own set of circumstances, health risks and goals etc. I couldn't possibly address individual needs in a book such as this, so I will use my own supplement program and treatment goals for demonstration purposes.

I'm 45 and except for a family history of cancer I fortunately don't have any other major risk factors and have enjoyed very good health to this point. As far as my goals are concerned, I want to remain healthy and not be restricted physically as I age. Having two young daughters I want to be able to play with them and with their children when the time comes. I see too many grandparents who can not participate as much as they would like due to a lack of energy or arthritis etc. In fact, I see parents that struggle to keep up. What are they going to do in 20, 30 or 40 years? A lack of vitality is truly limiting. I want to age gracefully and not succumb to the big three: cardiovascular disease, cancer and diabetes. I feel effective preventive medicine must contain a strategy on how to avoid premature death by the big three. Genetics largely determines how long we CAN live, but we continually sabotage the gifts of our parents with poor diet and lifestyle. The big three are to a large extent plagues of modern society. We are spending bizarre amounts on treatment relative to prevention. The big three have become industries unto themselves. To a large extent the big three CAN BE PREVENTED. I spend approx $125 Canadian dollars per month on supplements with the first $50 covering the two most important core items (multivitamin and Inositol + Cal Mag IP_6). Some people feel that this is a lot. It's truly a bargain to me. What's my health worth? Why do many of us insure our cars, but not ourselves? Cancer patients are often willing to sell everything including their homes, in order to have expensive treatments in America or overseas. I much prefer to prevent rather than to treat.

To prioritize then, my personal health goal is to first prevent cardio-

vascular disease, cancer and diabetes. Next I want to prevent arthritis. I would like to maintain overall vitality. I wish to have the best antioxidant for general anti-aging. Hopefully, by promoting overall vitality, use of chelators, potent antioxidants and by cardiovascular disease prevention I hope to keep my cognitive powers and prevent Alzheimer's disease as well. All this from a supplement program? No, but wouldn't it be nice! Supplements can however play a significant role. So here's what I take and very briefly why.

1st-Quality Multivitamin: Several benefits for overall health.

First and foremost is a quality multivitamin. A multivitamin is not where you should be shopping for a bargain. It surprises me how often people will only spend $5 on their multi, but $25 on an herb that they are not sure is even right for them.

2nd-Inositol + Cal Mag IP_6

1-Antioxidant for antiaging. Years ago prior to this supplement's availability, I was taking several antioxidants that are known to affect specific tissues. As IP_6 is essential and present natu rally in all of our cells it provides protection for all our tis sues. As an antioxidant it is considered to have an even more potent effect than even green tea. This is now my antioxidant of choice.

2-Cardiovascular support:

a-inhibits platelet aggregation, which is useful in stroke and heart attack prevention

b-chelator to prevent atherosclerosis or clogged arteries. Theoretically at least, this natural chelator could also protect against Alzheimer's. Recently (Dec 2003) the results of a clinical trial utilizing a new approach with a chelating agent (clioquinol) were reported. The trial demonstrated good initial success and a lot of potential for the use of chelators in the management of Alzheimer's disease.

c-preliminary evidence, is all-positive and indicates IP_6 may also help promote healthy cholesterol and blood pressure levels, but it is preliminary

3-Cancer preventative, extremely important with my family history

4-Diabetes prevention

5-Immune support (increases NK cell activity) therefore is useful to prevent the common cold and other viral diseases.

6-Bone density, as it is a highly absorbable source of calcium and magnesium

Note: This supplement has many applications, however personally I take it for the above reasons.

3rd-Glucosamine Sulfate and MSM for arthritis prevention

4th-Coenzyme Q10-Cardiovascular benefits

5th-Osteoprime which is a very comprehensive bone density or osteoporosis prevention product

6th-Ginkgo biloba (phytosome form) -peripheral circulation which affects memory and mental acuity

7th-Milk thistle (phytosome form)- I use it for 4 weeks each spring and fall as it helps with "cleansing" since it improves the liver's ability to detoxify.

Please keep in mind that this is my personal supplement program. Some might question the absence of flax or omega 3 oils. I have sushi weekly and my main source of protein is wild pacific salmon, which provides an ample supply of omega 3 oil.

The above reasoning almost makes Inositol + Cal Mag IP_6 sound like a panacea (good for every ailment). It's not, but it's as close as I've seen. This is why it is often referred to as the "Aspirin of the Twenty First Century". Most importantly it has real value when it comes to preventing our three biggest causes of mortality; heart disease, cancer and diabetes. I don't know of any other drug or natural medicine with as much preventive value for all three. For most preventative health programs I recommend it. However, there are two primary instances when I either don't suggest this supplement or am careful with its use in a preventative setting. First, with pregnancy it

has not been proven to be safe. It's probably safe as IP_6 occurs naturally in foods and inositol has a GRAS or Generally Regarded As Safe rating. However, probably isn't good enough when it comes to pregnancy. When my wife was pregnant I had her discontinue the supplement and instead encouraged her to eat foods containing IP_6 such as corn. Secondly, if a patient is on blood thinners or is scheduled for surgery, then because this supplement inhibits platelet aggregation I am careful and often discontinue or decrease the dose. In a healthy person, this would normally be considered a valuable effect, as drugs or natural products that help to inhibit platelet aggregation can help in the prevention of cardiovascular disease.

After deciding what supplements to use my next question then becomes "what about the quality of the product?" It's very troubling to me that we even have to ask this question.

With regard to brand, I feel that there are a number of quality brands when it comes to multivitamins. Multivitamins are well regulated in Canada and the U.S. with many of the ingredients assayed for purity and quantity. It's more a question of knowing what you want in a multivitamin, which is easily enough material for a another book. The greatest variation in quality occurs with herbal products.

I have chosen to use original suppliers of a product whenever possible for two reasons. First, I like to respect the efforts of those that are innovators, as they must overcome several obstacles in order to bring us new and improved medicines. It's no easy task, especially in the field of natural medicine when the companies don't have the deep pockets that the drug companies do. Secondly, companies that attempt to make a difference with innovative products usually are using the best quality material. It's the companies that copy or clone popular products that have a greater tendency to take short cuts on quality.

It's often difficult even for me to know the quality of products in the marketplace. Many companies are not large enough to have sophisticated in-house labs with analytical chemists to evaluate bulk product and outside assays are very expensive. In terms of quality, I don't see any easy answers for consumers. With so many brands

labeled the same how do you choose? I will use glucosamine as an example, as it has become very popular resulting in numerous brands and several quality control issues. If you pick inexpensive glucosamine are you sacrificing quality? If you pick an expensive glucosamine are you simply paying a premium? Generally you get what you pay for, but not always. When it comes to glucosamine, even the expensive products can be substandard. With glucosamine for example, it is believed that a number of companies have used excessive amounts of salt thereby diluting the glucosamine. Salt is necessary to stabilize glucosamine so that it can be used in capsule form, otherwise it absorbs too much moisture. Salt is far less expensive than glucosamine. By altering the relative ratio of glucosamine to salt a company can lower their cost. The diluted product may still improve a patient's symptoms, but likely not to the extent possible.

A number of companies truly go the extra mile to deliver great products, however there are those that don't and this has resulted in a tremendous variation in quality. Time and time again you will hear of studies that take random samples from various companies only to find many of the herbal products lack any active ingredient. A typical example occurred in Canada with St. John's Wort, where only 5 of the 12 sampled products demonstrated active ingredient. A typical clinical example occurs with saw palmetto, which is used for frequent nighttime urination in men due to an enlarged prostate. Men will try a brand for many months and experience no improvement. Then they switch brands and 3 or 4 weeks later they notice a dramatic change. Why? Most likely the first brand was of poor quality.

I've chosen not to mention what I feel are substandard companies, hoping instead that they will be weeded out naturally over time and to some extent this is already happening. Perhaps due to patient vulnerability, in the areas of weight loss, sexual performance and cancer there seem to be more products that can't live up to their hype, due to either poor quality or exaggerated claims.

Fortunately when it comes to Inositol + Cal Mag IP6 quality assurance is available in most western countries as the optimal ratio of IP6 to Inositol is protected by patent. If the bottle has the InoCell™ logo on it then the Cal Mag IP6 & inositol will be both of the highest

quality and also be in the optimal ratio. InoCell™ is the official distributor to the various vitamin companies of the patented Inositol + Cal Mag IP6. The Cal Mag IP6 used in the InoCell™ product is 98% pure with the other 2% made up of other phosphorylated inositols such as IP1 and IP2. Other companies are now distributing IP6 with grades as low as 50% purity. The problem is that the bottles will appear the same, only listing the milligrams of IP6 and not the purity. Again, very confusing for consumers. How does one even determine dosages? What's worse is that these companies will still not be able to combine IP6 and Inositol in the optimal ratio in many countries. Patients never come to me to get 50% better. Why should we even consider products with 50% purity? Natural medicine has so much to offer, but the industry's reputation is continually being tarnished by companies offering substandard medicines. Cancer patients for example, have so much to think about and simply shouldn't have to worry about poor quality medicines.

Another caution for consumers is the all too common practice of adding another product to an existing product in order to make a claim of superiority. These are often sold as "Super Strength" or "Mega Plus" type products. With glucosamine several years ago a number of companies added chondroitin to the formula, claiming a superior product. In fact the early chondroitin products were barely absorbable and in reality diluted the product when less glucosamine was used. They also relieved us of our cash, as chondroitin is far more expensive than glucosamine, even though it was far less effective. To an untrained person however, glucosamine with chondroitin sounds much more potent than glucosamine itself. The effect consumers felt was likely due primarily to the glucosamine and not the chondroitin.

Due to the potential value of Inositol + Cal Mag IP6 to support cancer patients, you can expect a number of "knock offs", once it gains some of the recognition that it deserves. With IP6 you can expect companies to start adding vitamin C or echinacea or mushroom extracts etc in order to make claims. Claims such as: "Superior Immune Fighting Power". Cancer patients are the most vulnerable of patients. They need to believe that there is something that can help them. They need hope, not false hope, but real hope. There are

those that will take advantage of these suffering people. It's unconscionable that this behavior exists, but it does. Just search the internet for cancer and immune boosters for evidence. There are serious potential problems with IP6 altered products. You'll likely not be getting the optimum ratio of inositol to IP6. The product essentially becomes a new product and as such is not likely to be supported by much if any scientific or clinical evidence. The most significant feature of Inositol + Cal Mag IP6 for cancer treatment is the ability to normalize the rate of cell division. It is not just the ability to boost NK cell activity. Increasing NK cell activity is possible with several products and just happens to be an added benefit, but certainly not the main benefit. In my case, would I even consider an altered product with echinacea or mushroom extracts etc on a long term basis? Of course not! That's not how these other herbs are intended to be used. As much as we want benefit, we must also weigh the risk(s): Does the long-term use of some of the added substance(s) pose any risk? Echinacea may help prevent the common cold, but is it safe or even logical when trying to prevent heart disease and diabetes as well?

Designing a supplement plan requires a clear definition of what you would like to achieve. For myself, it is first the avoidance of cancer, cardiovascular disease and diabetes. Once goals have been determined and the type of supplements selected, you will need to evaluate products for their purity and quality. This can be very confusing with so many choices available. Fortunately, as a result of proper patents, the chance of obtaining the best product is somewhat simpler with Inositol + Cal Mag IP6 (InoCell™), than it is for most other herbal or natural medicines.

Too Good to be True? Safe?

Is there a catch? With so many benefits is it just too good to be true? I expect that many of you reading this book are asking that very question. I would and I have! I posed this question when we introduced glucosamine and several other botanical medicines. I question all my patients as to how they're doing and any possible side effects, even when prescribed what are considered the safest of natural medicines. If I didn't constantly question safety, I wouldn't be doing my job. I am very pleased to tell you that as far as I can tell, Inositol + Cal Mag IP6 is a very safe product. A clinical setting is not the best place to test safety, but it is a good situation in which to screen for strange reactions none of which I have yet to see. Safety testing is best left to regulatory bodies as they consider evidence on a broad scale. Inositol is the molecule from which Cal Mag IP6 is made, and has been granted the GRAS status, which means it is Generally Regarded As Safe. In addition to some of the experiments and technologies described below, the GRAS designation is perhaps your greatest assurance of safety.

So many physicians consider medication for their patients using a benefit versus risk analysis, as they have come to expect that there is a down side to almost any medication. This is simply because most drugs are new molecules and as such the body perceives them as foreign or toxic, which then leads to side effects. I would guess that most physicians would have trouble even conceiving of a medication that only produced positive results. To make that leap many physicians would have to think of this molecule as a nutrient providing calcium, magnesium and inositol. Inositol + Cal Mag IP6 how-

ever, is much more, due largely to the fact that the phosphorylated inositols are necessary messengers within the cell and that the shape of the molecule enables it to function as both a chelator and potent antioxidant.

As inositol and the phosphorylated inositols (IP_1 to IP_6) are necessary and present in our blood, within all our cells and in several food sources, it's easy to see how a GRAS designation was achieved. The safety issue is really one of dose. How much can one take or how much should one take? These are the real questions. For preventive use at today's typical dosages of 1 or 2 grams daily, there is really very little need to be concerned. Dosage becomes a concern when a patient with metastatic cancer has a very poor prognosis and wants to take as much as possible. This is a tough call. We know from the Harvard study of kidney stones that took place more than 40 years ago, that a dose of 8.8 grams daily in divided doses resulted in no side effects or problems for patients taking the medicine for up to 2 years. Can we give more safely? I don't really know, but suspect based on statistics that showed that South African blacks receive up to 40.8 grams of IP_6 daily when consuming 680 grams of corn, that yes, perhaps we can go higher. However, there is an important distinction to keep in mind when comparing a food versus a supplement source of IP_6. As a supplement the absorption is much higher, especially if taken between meals. And then there is a question of risk versus benefit: is the benefit of treating metastatic cancer worth the risk of any putative negative side effect?

The Finnish people offer further evidence as to safety. According to Weisburger et al., 1993: "The Finnish people have a low colon cancer rate and a lower breast cancer rate than Europeans and Americans, generally because of a high cereal insoluble fiber intake, and these populations do not display any signs of mineral or vitamin deficiencies leading to abnormal growth and development".

The most consistent concern that I hear, is a fear that the molecule could potentially cause osteoporosis because of its mineral binding or chelating properties. This fortunately need not be a concern and in fact the opposite should be the case, if one is using the correct form of IP_6. The type of IP_6 used by InoCell™ (Cal Mag IP_6) is

bound to 6 atoms of calcium and magnesium, whereas some IP_6 is bound to iron or sodium etc. In essence the right IP_6 will deliver a substantial amount of highly absorbable calcium and magnesium.

To further put the bone density issue to rest, one only needs to realize what happens to IP_6 once ingested. The majority of the molecule is actually broken down to carbon dioxide (CO_2) and expired out the lungs. When exchanged as a gas there is no way for the metabolized broken down molecule to bind minerals. An elaborate study was conducted to investigate IP_6 breakdown and helped to establish this very point. Researchers painstakingly grafted radioactive carbon 14 (C14) into young wheat plants as part of inositol molecules, which the wheat then converted to C14 containing IP_6. Then the radioactive IP_6 was given to rats as part of their food. Being radioactive the researchers were now able to trace the IP_6 movement within the rats. They found that over half of the absorbed IP_6 left via the lungs as CO_2. At the same time the researchers varied the calcium in the rat's diet. Amazingly the lower the calcium in the diet the more IP_6 was absorbed, as if bodies instinctively know what to do.

Binding of minerals does take place, as evidenced by the ability of IP_6 to prevent kidney stones. However, only a very small percentage (some estimates are 1 to 3%) actually exits via the kidneys. Even if we assume that the higher 3% of IP_6 leaves via the kidneys, it works out that for every 33 atoms of calcium or magnesium brought into the body by IP_6, only one can be removed by being bound and taken out via the urine. In other words at the very least, the molecule brings in 33 times as much calcium in as it can take out. One needs to keep in mind that in addition to leaving via the lungs or exiting via the kidneys that in fact, much of the IP_6 is taken up and used by our cells.

In terms of acute toxicity, the use of IP_6 in several diagnostic imaging techniques provides further evidence as to its safety. There is little chance these techniques would allow IP_6 to be ingested or injected if it was not found to be safe. In use for over 30 years, IP_6 is now used extensively around the planet in diagnostic radiology. IP_6 is bound to various molecules such as Technetium 99, helping them to travel to various organs such as the spleen or liver.

I have found little reason to be concerned about toxicity or side effects from IP6 at preventive dosages (as above), but I am cautious of its use in two primary instances. The first is with pregnancy. Many drugs are not tested on pregnant women just in case a problem occurs, because if problems do occur, the lawsuits could be enormous. The result is that physicians often have to use their clinical judgment when it comes to prescribing during pregnancy. When it comes to IP6, even though most women receive some in their diets, and even though inositol is believed to potentially prevent neural tube defects and diabetic embryopathy, the fact is that IP6 has not been tested as a supplement during pregnancy. As I stated in the "Designing an Optimal Supplement" chapter, I had my wife discontinue the supplement when she was pregnant. Instead, I encouraged her to eat IP6 containing foods such as corn. The other instance in which I typically have patients discontinue or reduce their IP6 intake is when they are on blood thinners or are scheduled for surgery. IP6 does not "thin the blood" per se, but instead inhibits platelet aggregation or "stickiness" so that less clotting occurs in the blood vessels. This is normally a desired effect as it can help to prevent heart disease. However, in the case of a surgery for example, one must be careful to avoid anything that can cause excess bleeding.

Inositol is the first half of the "Inositol + Cal Mag IP6" supplement. It also provides the base structure for the Cal Mag IP6 and is often referred to as the mother of IP6. They are combined together in the same formula, as they have been proven in a number of research studies to complement and augment each other's effects. The Physicians' Desk Reference Family Guide to Nutrition and Health (1995) says that inositol has not been found to be toxic at any dosage level. Michael Lesser, M.D. has stated that: "as much as 50 grams (50.000milligrams) has been taken by mouth with no ill effect."

Inositol + Cal Mag IP6 is surely one of our finest, if not the finest, general use preventive medicine available today. This rice extract does a fine job in keeping to one of the fundamental principals of Naturopathic Medicine, which is: First Do No Harm.

Final Comments:

Prevention • Prevention • Prevention!

Years ago I made a personal commitment to do whatever I could to increase the awareness of Inositol + Cal-Mag IP6. I have always been excited about sharing information and research about this supplement. At the same time I am saddened that after 6 years of its being available, I felt compelled to write this book. I had truly hoped by now that it would be our most popular preventive medicine based on its remarkable ability to prevent cancer, not to mention its role in bone density, heart disease, diabetes, mood disorders, kidney stones, immune support and as a potent antioxidant. It's a similar frustration knowing how long it's taking for Dr. Shamsuddin's early stage cancer detection tests to become available. How many hundreds of thousands of lives could have been saved if patients had their cancer found prior to spreading?

Natural medicine is becoming very popular, however it is common to have it confused with preventive medicine. Many people believe that as a Naturopathic Physician and Doctor of Traditional Chinese Medicine that I primarily practice preventive medicine. I do of course whenever I get the chance. However, to gain this opportunity it's necessary to first help patients with their pain or discomfort and address why they initially came to the clinic. I applaud those that do, but unfortunately it's uncommon for healthy patients to book appointments purely with a desire to learn how to stay that way. Centuries ago in China the medical system was very interesting. Physicians were paid only when patients remained healthy and therefore truly did practice preventive medicine. I believe that it's largely human nature that we don't think about our health until it fails us. I can't tell you how many cancer patients would go back and make changes if they only could. How heart wrenching it is to witness someone gasping for air, grimacing in pain or to see the grief and sadness cancer brings to families. I know it can be difficult to convince and continually motivate someone to incorporate a supplement into a health program on a long term basis, especially if they are not actually treating a disease. Hopefully the avoidance of cancer will provide the motivation. Hopefully at least a small fraction of the billions and billions spent on cancer treatment will go towards prevention. Hopefully we will realize sooner rather than later that the easiest way to win the war on cancer is to prevent it.

Metabolism

Ivana Vucenik Ph.D.

IP_6 and Inositol are Common Molecules of Plants, Animals and Humans

IP_6 and Inositol (Ins) are widely distributed among plant and animal kingdom. As important dietary components for humans, IP_6 has been known from ancient ages. High amounts of this substance are present in rice, corn, beans, whole-grain cereals, non-refined cereals derivatives, and all types of nuts, in concentrations from 0.4 – 6.0% [Harland et al, Reddy et al]. However not only plants but almost all animal and human cells and tissues contain IP_6, although in much lower concentrations (~100,000 times less); in human blood (plasma) and urine IP_6 content is ~ 0.2 mg/L. Tissues in general contain more IP_6 than plasma. The highest IP_6 concentrations were found in brain, whereas the amounts found in kidneys, liver and bone were similar to each other, and 10-fold less than those detected in the brain. The IP_6 levels in human cells (cultured cell lines) are similar to those detected in tissues, and about 50-fold higher than levels found in plasma or urine [Grases et al]. Both IP_6 and Ins are essential for key body function. Thus, free Ins is also found in blood and in almost every cell and tissue in our organism. High levels of Ins are found in brain and in seminal fluid, because the nervous system and reproductive organs depend on a constant supply of Ins.

Until recently, a majority of data related to cellular IP_6 content has been evaluated through cell cultures and radioactive measurements after long-term culture with radioactive Ins (7 days). A missing clue to the possible importance and functions of IP_6 was the determination of its natural and physiological levels in different mammalian tissues. Novel methods for measurements of IP_6 in biological samples have permitted the evaluation of the total amount of IP_6 present in tissues and biological fluids of humans and animals [Grases et al].

IP_6 Metabolism

To better understand the mechanisms of action and to properly design clinical trials of IP_6, it was crucially important that the absorption, metabolism, tissue distribution and excretion of IP_6 be known. In general, IP_6 degradation is a rapid process, while its synthesis is very slow.

Ins has a core [carbohydrate] structure identical to IP_6, minus the phosphates (please see Figure 1); thus, Ins is a backbone molecule, a "mother" of IP_6. With small changes in its chemical structure, such as addition of phosphate groups, from one to six, a whole "family" of inositol phosphates (IPs), all active molecules, can be formed. IP_6 molecule is rapidly degraded by the enzyme phytase by losing one or more phosphate groups from the Ins ring (please see Figure 1), generating IP_5, IP_4, IP_3, IP_2, IP_1 ($IP_{1\text{-}5}$) and Ins. Thus, IP_6 can revert to Ins by losing phosphate groups, and Ins can be converted back to IP_6 by gaining phosphate groups. So this is a case of chicken and egg scenario. Although, there are multiple effects of both IP_6 and Ins for human health, IP_6 and Ins are synergistic in these health effects; the combination of IP_6 and Ins is more effective than each component alone [Vucenik et al].

In rats, radio-labeled IP_6 was found to be quickly absorbed from the stomach and distributed through the body [Grases et al]. Likewise, IP_6 is also quickly absorbed and metabolized by cancer cells: IP_6 is rapidly taken up my malignant cells and dephosphorylated into inositol phosphates with fewer phosphate groups ($IP_{1\text{-}5}$) [Sakamoto et al]. Orally administered IP_6 can reach target tumor tissue distant from the gastrointestinal tract. When radio-labeled IP_6 was given to animals bearing mammary tumors, a substantial amount (20%) of IP_6-associated radioactivity was found in tumor tissue as early as 1 hour after administration, clearly providing at least in part an explanation for the anti-neoplastic activity of IP_6 at sites distant from the gastrointestinal tract. It was shown that 50% of the radioactivity was excreted in urine within 72 hours, feces accounted for another 10 % of radioactivity, suggesting that at least 40% of the IP_6-associated activity was distributed within the animal tissues [Vucenik et al]. These experimental data indicate that IP_6 can reach and concentrate

at cellular targets. It was found that tumor tissue contain Ins and IP_1, similar to plasma, as a result of a rapid metabolism.

Using novel and more sensitive methods for determination of non-radio-labeled IP_6 in biological fluids, it was possible to study the pharmacokinetic profile of IP_6 in rats, and for the first time in humans, important to clarify its absorption and excretion [Grases et al]. More importantly, it was possible to measure the real concentration of IP_6 and inositol phosphates with fewer phosphate groups (lower IPs) in biological fluids and tissues as they are. Orally administered IP_6 is excreted in urine. The urinary level declines when IP_6 is withheld, and increases with an increasing amount of ingested IP_6, reaching a peak excretion level which is not further increased by ingestion of additional quantities of IP_6. After 2 weeks of consuming a diet totally deprived of IP_6 (cereal derivatives and other vegetable seeds, legumes and nuts), the plasma and urinary levels of IP_6 decrease to around 75%-80% of the normal values found in humans. Similar data was observed in rats. After fasting, IP_6 was quickly absorbed, reaching the maximum concentrations in plasma as early as 4 hours after ingestion of pure IP_6 as supplement. On the other hand, it took a long time (more than 10 days) for the IP_6 level to come back to normal level when IP_6-rich diet was eaten [Grases et al]. A similar relationship between the dietary ingestion of IP_6 and its levels in the biological fluids and tissues was observed also in rats.

IP_6 was found in substantial amounts in mammalian cells, ranging from 0.01 to 1 mM. It is important to note that concentrations have been found using cultures of different cell types treated by radio-labeled Ins in medium and by determination of formed cellular radioactive IP_6. However, the problem with these methods is the IP_6 pool incorporates radioactive Ins so slowly that it takes more than 7 days and the radioactivity itself may be responsible for cell stimulation, but the most important is that a part of IP_6 may be still bound to membranes and proteins, and it is not clear how much IP_6 is really freely soluble. Thus, although it has been indicated that IP_6 can be synthesized from Ins, it is a very slow and complex process, needing more than 7 days, multiple steps, and the hard work of enzymes called kinases to attach the phosphate groups to the Ins backbone. Therefore, IP_6 synthesis has been studied in model systems outside

of humans or the animal kingdom, in a slime mold Dyctiostelium discoideum, and in yeast, and the controversy about synthesis of IP_6 in human and animal cells still continues. However, it has been recently demonstrated that the majority of IP_6 found in organs and tissues has a dietary origin and is not a consequence of endogenous synthesis. Thus Dr. Shamsuddin's original working hypothesis that the dietary IP_6 that is the source of intracellular IP_3 appears to be correct. IP_6 must therefore be supplied by food and supplements to maintain adequate levels in different organs and tissues for healthy living [Grases et al, Grases et al].

Although there are still some uncertainties about IP_6 synthesis in vivo, it is clear that IP_6 is a molecule that can be rapidly dephosphorylated to lower IPs. However, at this moment we are not sure whether it is only IP_6 or its metabolites, Ins and/or $IP_{1\text{-}5}$ that are biologically active in providing protection for human health. Further work is clearly needed.

IP_6 a Vitamin?

Ivana Vucenik Ph.D.

Can IP_6 be considered as a new vitamin?

Its precursor Ins is a member of the B complex family of vitamin. Ins has been granted the GRAS status (generally regarded as safe).

What are vitamins?

Vitamins are a group of substances that help regulate metabolism and are essential for normal cellular function, growth and development, and general well-being. All natural vitamins are organic food substances found only in plants and animals, and required by humans in small amounts. With few exceptions, the body cannot manufacture or synthesize vitamins. They must be supplied in the diet or in dietary supplements. Each vitamin has specific function. An organic compound is considered a vitamin if a deficiency disease results when the levels of that vitamin in diet are inadequate.

Both IP_6 and Ins are essential to the normal functioning of our bodies and for a healthy life. A lack of IP_6 and Ins in the diet results in overt symptoms of deficiency. IP_6 is a strong antioxidant, has a power to prevent and fight cancer, can prevent development of kidney stones, fatty liver can increase resistance to infection, and can reduce key factors for heart disease, such as increased lipids and platelet activation. On the other hand, Ins is useful in treatment of psychiatric disorders, and is effective in preventing many of complications associated with diabetes mellitus.

IP_6 and Ins are widespread in plant kingdom, and have been dietary components of animals and humans from ancient ages. Very recently it has been clearly demonstrated that the majority of IP_6 found in organs and tissues has a dietary origin and is not a consequence of endogenous synthesis. Thus, IP_6 must be supplied through food and supplements to maintain adequate levels in different organs and tissues.

IP_6 content in a healthy and recommended diet, such as the Mediterranean diet, ranges between 0.7-1.4 g/day. It is important to note that dietary habits in developed countries tend to eliminate IP_6 from meals due to reduced consumption of whole grain foods, legumes and nuts. Not to mention the Atkins diet, and the explosion of other various “low-carb” diets as fashionable tendencies today in the USA. Thus, to maintain the appropriate IP_6 levels, the consumption of IP_6 supplements is necessary when the diet is poor in IP_6. For Ins, it is estimated that adult humans consume approximately 1 g per day from plant sources and animal products.

IP_6 does not adversely affect the normal levels of minerals in our body, as blamed by some nutritionist; on the contrary, it prevents abnormal and pathological mineralization, as shown by the enormous work of Prof. Felix Grases and his group [8]. And, IP_6 normalizes abnormal cell growth and function, as shown by Prof. A.K.M. Shamsuddin and his group [6].

Experiments have demonstrated that the absence of IP_6 in rat’s food provoked the development of pathological calcification in the kidneys [starting of stone formation] of rats that were prevented with IP_6 addition to diet. The development of calcifications was also accompanied by anomalous calcium accumulation in rat kidneys that was significantly reduced in rats fed on IP_6-rich diet. Low values of urinary IP_6 were also detected in a group of oxalocalcic stone-formers when compared with urinary levels observed in healthy subjects. Similar to kidney stone development, tumor formation, either chemically induced or spontaneously appearing, was also significantly reduced when IP_6 was present in drinking water.

Urinary and plasma levels of IP_6 are related to its oral intake through the diet, with levels going down following ingestion of an IP_6-poor diet, and returning back to basal levels after resumption of an IP_6-normal diet, or ingestion of dietary supplements. Thus, urinary IP_6 level can be considered a marker of a deficiency or sufficiency.

IP_6 is involved in the control of so many important physiological processes inside and outside of our cells, and the value of adequate diet and supplements in supplying this substance is obvious.

The (a) natural occurrence of IP_6 in our diet, (b) its ubiquitous and physiological presence in our body at low levels, (c) levels which fluctuate with its intake, (d) the positive roles of IP_6 for human health, (e) association of an IP_6-rich diet with low incidence of several diseases, as well as (f) relation between an IP_6-poor diet with high incidence of some diseases and the reversal of some of these condition, at least in part, by IP_6 supplementation are criteria befitting a vitamin.

Ironically, blamed for many years as an anti-nutrient, this evidence strongly argue in favor of its inclusion as an essential nutrient or perhaps a vitamin.

Frequently Asked Questions

1-Is Inositol + Cal Mag IP6 safe?
This rice bran extract is a very safe food based supplement. However, there are two main instances when I exercise caution and discontinue or lower the dosage. The first is with pregnancy, as it has not been tested specifically with expectant mothers. The second is with patients who are on blood thinners or are expecting to have an operation, as the supplement inhibits platelet aggregation. Please see the Safety chapter.

2-Do I need to be concerned about bone density, since this supplement is known to chelate minerals such as calcium?
No, if anything Inositol + Cal Mag IP6 delivers far more calcium and magnesium than it can remove. Cal Mag IP6 is just that, calcium and magnesium bound to IP6. Even at conservative estimates, the supplement would supply 33 times more calcium than it can remove. Please see the Osteoporosis chapter.

3-Why is inositol added to Cal Mag IP6 in the same formula?
They are combined because the two molecules are similar and complement each other's functions in several areas of our physiology. The combination of the two has been proven to provide a more powerful immune response than either molecule alone. In addition the molecule inositol triphosphate or IP3 is known to have a normalizing impact on the rate of cell division. By combining inositol with Cal Mag IP6, we can double the potential IP3 content.

4-Can I take this supplement if I am receiving chemotherapy?
A number of chemotherapy agents work to destroy cancer cells by

oxidizing them. As a potent antioxidant there is some concern about IP_6 neutralizing the action of the chemotherapeutic drugs. This is a theoretical point that is often raised about antioxidants in general. I am not aware of any clinical trials with antioxidants to test this concern. My feeling is that antioxidants help rather than hurt in this situation, but this is only my sense and I can not offer any proof. As a precaution with patients, if they are receiving an oxidizing type of chemo, I have them stop the antioxidants for a few days before and after the chemo. Theoretically this supplement should complement the effectiveness of chemo. The hope is that the chemo will kill the majority of the cancer cells and that the supplement taken between the chemo treatments will help to control the rate of cell division of the cancer cells that survived the chemo. In this way, when the chemo is next administered, hopefully there will be fewer cancer cells that need to be destroyed. This supplement was in fact tested with two common chemo drugs; Tamoxifen and Adriamycin and was shown to augment the effectiveness of both drugs without increasing their toxicity. See the Cancer chapter.

5-What about dosage?
For a healthy adult 1 to 2 grams daily (This would be approx 2 to 4 capsules from most vitamin companies) is recommended for preventative purposes. Up to 8.8 grams of IP_6 were used safely for an extended time period (please see the Kidney Stone chapter). Up to 50 grams or 50,000 milligrams daily of straight inositol did not produce any unwanted affects. The question becomes; can one take more than 8.8 grams safely? The answer is uncertain, because this hasn't been evaluated clinically. Please see the Safety chapter for more details.

6-Is it best taken with food or on an empty stomach?
The difference between the two scenarios would be the amount absorbed. On an empty stomach you can expect a higher absorbency rate.

7-Do I take the supplement myself and if so how much?
Absolutely, especially with my family history of cancer. However, when you think of it, approximately one in three will get cancer and so we're really all at risk. Please see the Designing an Optimal Supplement Chapter. The supplement comes in two forms, as a capsule or as a powder. Personally, I like to use the powder on my oatmeal each morning. Remember that inositol is often derived from glucose, so in effect I use it as a sweetener. In capsule form I often recommend taking 3 or 4 capsules daily for prevention on an empty stomach. Since I use mine with food, I up the dose slightly to the equivalent of approx 5 or 6 capsules, or in my case three quarters of a scoop. The scoop I am using holds approximately 8 capsules.

Cancer Testimonials

Treating cancer is difficult. I am not intending to create any false illusions by sharing these testimonials. However, I do think it's important to include them, because a number of patients are somehow beating the odds and we must always ask ourselves why. I believe that this supplement provides some legitimate hope for cancer patients. Even a little bit of legitimate hope can make a huge difference for those suffering.

I learned of perhaps the most astounding case while doing a general immune system lecture for pharmacy and health store personnel in the summer of 2002. After the talk, a semi-retired medical doctor stayed behind to tell me his wife's story. Four years earlier in 1998 his wife was diagnosed with very advanced pancreatic cancer and was told she only had a few weeks to live. She is a tall woman and had shrunk down to 85 pounds. In desperation they decided that she should try some natural supplements, which included Inositol + Cal-Mag IP6. He was excited to tell me that she was doing fine and now weighed 120 pounds. Never having called him before, a few months ago I got his phone number from the health food store from which he buys his supplements. I called and asked for the doctor. An elderly lady answered the call and I then described why I was calling. She was more than pleased to tell me that she was in fact the pancreatic cancer patient and that the doctor was her husband and most importantly that she was doing great almost six years later!

Dr. Shamsuddin told me of another inspiring story. A lady in his mother's nearby neighborhood in Dhaka, Bangladesh had advanced lymphoma. She traveled to India to get a second opinion at one of India's top facilities and was told she only had 6 to 8 weeks as her

body was full of cancer cells. Coincidentally, immediately following the First International Symposium on IP6 in Kyoto in June 1998, one of her sons learned of Dr. Shamsuddin and IP6 through press reports and Internet search. Not even knowing that Dr. Shamsuddin grew up 3-4 blocks away, he sent him an e-mail to the University of Maryland in Baltimore. Out of desperation and in spite of the ridicule of her local oncologists, she was placed on Inositol + Cal-Mag IP6 [because of the distance, the first few samples of Inositol + Cal-Mag IP6 came from Dr. Shamsuddin's mother's supply who was by this time taking her son's medicine religiously!] Two years later when Dr. Shamsuddin was visiting his mother there was a knock at the door, standing there were the lady's two sons with an enormous bouquet in appreciation. Remarkably she was now considered cancer free. She had returned to the same clinic in India for a follow up, but the laboratory [biopsy] reports were not given to her. Initially she was denied the lab reports as they thought there must be some mistake, how could she be the same woman since she didn't have any cancer cells the lab could identify!

I recall a very similar situation with my mother, whom I had mentioned earlier and who had Hodgkin's lymphoma. After returning from a healing ceremony with a Native American shaman, my mother's oncologist was baffled and wondered if initially he had made a mistake. My mother's cancer was regressing and this just didn't make sense according to the doctor.

I would encourage all of you to submit your experience with Inositol + Cal Mag IP6 to www.ip6.info so that a comprehensive data base can be developed. Or if you prefer, my clinic number is 1-604-913-1110 and I will help to facilitate getting your information added to the database. Health food stores normally are not able legally to keep patient records. This makes this process more difficult than with prescription drugs. All your cases are valuable, whether you had a positive result or not. From osteoporotic to diabetic to cancer patients etc, all of your information can be used to ultimately help others. Most importantly, individual case studies will help scientists design clinical trials to further test this nutrient.

Testimonials

Lisa B. of Chicago was diagnosed with breast cancer at age 35. An attractive, athletic person, who worked as a personal trainer, she confronted the disease head on with confidence. Following breast cancer surgery in January, 2003, she went through a series of chemotherapy and radiation treatments. By the end of the summer her recovery was progressing nicely. However, in early September she began experiencing severe headaches. A brain scan showed a tiny spot that her doctor thought was insignificant. An MRI conducted two weeks later revealed that Lisa had cancer in the lining of her brain and in her spine-a condition known as Leptomeningeal Disease. Within three days of this diagnosis, Lisa was placed in intensive care. She eventually lapsed into a coma, and became paralyzed. A feeding tube was inserted to provide her with nourishment. Doctors, once again, administered radiation to combat the cancer, but it didn't seem to help. After consultation with other hospitals, they began a more aggressive treatment with chemotherapy and a new cancer drug, Temodar. They told Lisa's mother, Joan, that her daughter could expect to survive three to six months with this treatment, and that most people usually die once they go into a coma. Joan insisted that doctors also treat her daughter with an alternative therapy, IP6, (Inositol Hexaphosphate plus Inositol), a powerful antioxidant derived from Vitamin B that promotes healthy cell function. Joan had first learned of IP6 when her mother contracted lung cancer. In addition to her mother's conventional treatment with chemotherapy, Joan made sure her 78-year-old mother got healthy doses of IP6. Her mother beat the lung cancer and is still living today at age 84. While doctors were not optimistic about Lisa's recovery, she soon began to show signs of improvement. Much to their surprise, she emerged from the coma, and began to show dramatic signs of improvement. An MRI conducted at the end of October showed no signs of cancer. Today, she is home and walking again-although slowly. She appears to be on the road to a complete recovery. Her doctors find her recovery hard to explain, but Joan feels that IP6 played an important role. "I would like to see doctors learn more about natural products like IP6 that don't have the side effects of heavy drugs," she says.

At last--someone who has used IP6. Last April my husband was diagnosed with cholangiocarcinoma, a liver bile duct cancer, and was given a prognosis of 6 months. He is still with us after nine. He began taking IP6 in June of 1998 and has been on a dosage of 4 capsules 2 times a day. My husband is a wonderful father, husband, and grandfather and I pursue any lead to help him survive this devastating disease. He has other health problems that have made his cancer difficult to treat, but he did undergo 6 weeks of combined radiation and chemo. We have been told that there are no longer any signs of the tumor and it will be a true test of the IP6 if regrowth or spread of the cancer can be prevented.

Karen G.

In mid-summer 2002, I noticed that the area around my stomach was growing larger. At first I attributed this to normal weight gain, but I noticed something was wrong after I began eating more healthy foods and the bloating still wasn't going away. As time passed I became more uncomfortable, so I went to my practitioner of Tibetan medicine. She said the problem could be very serious and recommended immediate testing. In August I went to the hospital emergency room, and after several tests, the attending doctor told me I had cancer. Additional testing diagnosed it as stage 3C ovarian cancer.

In September I underwent surgery. A majority of the tumors were removed, but 20 percent remained. At around this time a friend of mine recommended IP6 to me based on the success of a friend of hers. I did some research, and began taking 6 pills a day on October 29. My condition began to worsen so I started chemotherapy on November 7. I was given carbo platinum, which made me so sick I was hospitalized. A week later I started feeling much better, and my CA125 (which is a cancer blood marker) went from 2,600 before surgery to 215 on November 19. On December it dropped to 63.9. My doctor was amazed and attributed my turnaround to IP6. As of January 14, my CA125 was 19.6 (the normal range is 0-35). I had an ultrasound on January 10 and the remaining tumors were gone. I am now in complete remission. Considering the grim statistics on Stage 3C Ovarian Cancer (the average 5 year survival rate is only 10%), this is truly astounding.

Aside from IP6 (which I have upped to 12 pills a day), I started taking green tea extract, grape seed extract and Quercetin in December. In January I added Bromelaid, Fish Oil pills, Immunocal and freshly juiced carrot, celery, apple, kale and parsley juice. And from the beginning I have had many prayers said for me and have done daily meditations. I also have a fierce determination to survive. I feel that all of these factors have contributed to my recovery, particularly the total support of my doctor.

Grace Tarrabay.

I'm a retired lieutenant from the FDNY and on September 26, 2002 I was diagnosed with High Grade Prostatic Intraepithelial Neoplasia (PIN), which my urologist told me is associated with prostate cancer in approximately 30-50% of men who demonstrate this finding. I was told a repeat needle biopsy would be required in 3 months.

I had been taking IP6 since January, 1999 on a maintenance level. Although I had this condition (PIN), my overall health is fantastic. I contacted Dr. Shamsuddin and told him I was going to increase my dosage of IP6 to the level of one at "high risk" for cancer.

On January 9, 2003, I had another needle biopsy. All eight specimens of the prostate were benign prostate tissue and there was no evidence of malignancy. In short, the PIN cells were gone!

As a man of deep faith, I know that the Lord Jesus used IP6 to clear up the condition for His glory and my good. My sincere thanks and appreciation go out to Dr. AbulKalam M. Shamsuddin.

Rev. J. Caterino

I was diagnosed with a multifocal hepatocellular carcinoma, secondary to chronic Hepatitis C, in August of last year. I received no conventional therapy due to this being a multifocal scattering of tiny tumors throughout my liver, with one larger tumor measuring 2cm. The oncologists sent me home and told me to come back for pain management when necessary. I became aware of IP6 first through a physician friend and then on a television show. I started taking it in the latter part of last year, not really convinced that it would do me any good but willing to try anything. Subsequently all of the smaller tumors have been resolved and the larger tumor was handled with alcohol ablation. After two treatments with alcohol I appear to be tumor free. I plan to continue IP6 for as long as I reside on this planet.

Bob S.

I have been using IP6 (8 capsules, twice/day) for 3 weeks (I have a bizarre form of cancer, and am just using IP6 along with nutrition). I have gained 5 lbs. and am sleeping better than I have in a long time. I called Dr. Shamsuddin at the University of Maryland, and he spent 40 min talking with me. He truly seems like a caring, wonderful man. He said he did not publish all of his findings in his book, as he was afraid people would find it too incredible to believe. He said to take 8 caps, twice a day on empty stomach for cancer. When cancer is gone, then take 3 or 4 caps, twice a day. I would be most grateful if you could put me in touch with other IP6 users, so we can share information.

Fred P.

My dad is a survivor thanks to IP6! He found out in December 98, he had 75 lesions on his liver. Instead of panicking, we did our homework. We found out about IP6 and he started taking it daily. Since August '99 he is free from cancer. He now takes it as a preventative daily and so does the rest of my family.

Suzie

I started my fiancee on IP6 in May; in January his PSA was 13 and climbing, in August his PSA went to 9 and now is 0.6. We're ecstatic! All I know about IP6 I read in the IP6 cancer book by Dr. Shamsuddin. IP6 is just inositol (Vitamin B) with six phosphates attached. The IP6 book says that IP6 normalizes cancer cells and allows them to die. The IP6 book says that there seems to be no known toxic level for IP6 or inositol. IP6 has been tested for cancer on animals for over thirty years. The reason that IP6 did not receive much attention was the concern that IP6 would remove minerals from the blood stream. Tests have recently proven this about IP6 to be false. The IP6 cancer book does mention on page 89 that tests show that IP6 was able to remove the calcification in arteries of test animals. The part that I like about IP6 is that it can help prevent cancer, or at least IP6 can reduce the number and size of tumors.

Winnie

My mom has been using IP6 since May 1999 for a Glio4 brain tumor and it has been helping her. The tumor was downgraded in July 1999 and then in December 1999 we were told it hadn't grown since July. The doctors had no explanation other than to keep doing what we are doing and we are. For a tumor such as my mom's not to grow is highly unusual. She was supposed to die over a year ago. She was diagnosed in December 1998. We know of two other people who have used IP6 with tremendous results. One woman had two inoperable Glio4 brain tumors being diagnosed in November 1997 and was prepared to die, but was started on IP6 by some church friends sometime in 1998. After a time the tumors stopped growing and they have been shrinking with each MRI done. I was so glad to hear of the success with IP6. Thanks.

Martin K.

I have had Non-Hodgkin lymphoma low-grade type for five years. I underwent conventional treatment during that period. I have been using IP6 since December 1998 and have had dramatic results. My tumors have reduced in size by about 80%. I would be interested in communicating with other people that are taking IP6 for cancer.

James B.

My wife is using IP6 (Cell Forte™ brand) with great success! She had a cancerous tumor in her breast that was removed. She started IP6 about 6 weeks before the surgery and after the surgery all lab results showed clean margins and negative nodes. This was very surprising to the Surgeon and Oncologist due to the size of her tumor (3.2cm+).

Jim B.

Four years ago our daughter Lindsay, who was 15 years old, began having severe headaches from which there seemed to be no relief. After consulting a pediatric neurosurgeon, we learned that Linsday

had a walnut-sized brain tumor on her brain stem which would require surgery in two weeks. We were told to prepare for a lengthy recovering period to follow.

Previously we met Dr. Shamsuddin at a book signing of his book on IP6. We made contact with him to learn more about the product and its potential to help Lindsay's condition. I also learned about case studies of other cancer patients who had taken IP6 and experienced very positive results. Immediately thereafter I began giving Lindsay 8 capsules of IP6 twice daily, for a total of 16 capsules per day.

Less than 24 hours before Lindsay's scheduled surgery, the neurosurgeon reviewed her case with a panel of the best surgeons in the country, and, to our delight, he found that the operation was no longer necessary. We went home knowing that she would not have to endure surgery, but would have to undergo a six-week course of radiation therapy.

During the course of radiation treatment, I prepared IP6 in juice every morning for Lindsay, and made sure she took her full dosage of 16 capsules a day. I even baked IP6 into batches of cookies to make it more enjoyable for Lindsay to take. After 8 weeks, and another MRI to check the tumor's growth, we were thrilled to learn that Lindsay's tumor had "unexplainedly" shrunk by 22%! The doctors were absolutely amazed.

I am happy to say that Lindsay is now a healthy, 19-year-old college student with a career in music ahead of her. She continues to take IP6 daily. In addition, I've continued to work and rework the IP6 cookie recipe, and now have four different varieties of wheat-free, gluten-free cookies with the IP6 equivalent of 2 capsules for cookie.

Sheri F.

References

Research investigating inositol and IP6 has increased tremendously in the last decade. To get a sense of just how interested scientists are, the number of scientific papers that have been published and registered with PubMed as of mid May 2004 are listed below. You can look up the abstracts yourself at www.pubmed.com. You will see far more studies regarding inositol than inositol hexaphosphate (IP6), which one would expect, since inositol is one of the main molecules or components of cell membranes.

Unlike internet search engines such as Google, the results below are not duplicated. Therefore, if the number is 100, then it implies 100 unique papers have been published. PubMed lists the studies in chronological order, with the most recent studies first.

Search Term(s)	Number of Papers
Inositol	27,114
Inositol and Diabetes	841
Inositol and Neuropathy	185
Inositol and Depression	277
Inositol and Cholesterol	326
Inositol and Pregnancy	488
Inositol and Antioxidant	397
Inositol and Cancer	2,159
Inositol Hexaphosphate (IP6)	1,817

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About the Authors:

Dr. Kim Vanderlinden practices at the Ocean Walk Medical Centre in West Vancouver, Canada. Ocean Walk is Vancouver's first integrated health clinic. With degrees in both Naturopathic and Chinese medicine, he provides a unique approach for patients that includes both Western and Eastern perspectives.

A former instructor at the International College of Traditional Chinese Medicine, he lectured on the integration of Naturopathic and Chinese herbal medicine within the western medical model. As an educator, he has lectured and written articles helping with the initial introduction into Canada of several of the most useful natural medicines such as: glucosamine, saw palmetto, St. John's Wort, black cohosh and DGL etc. Dr. Vanderlinden also co-introduced ozone therapy, a new, non-surgical treatment for herniated discs, into Canada.

Believing in the power of informed consumers, Dr. Vanderlinden founded Medicine.info, which is an internet medical portal with hundreds of individual condition and treatment websites all linked to the main site at www.Medicine.info. Presently missing on the internet is a central site that provides an integrated, balanced approach to conditions encompassing both western and evidence based natural medicine. It is to be launched in 2005.

Dr. Vanderlinden is presently developing the foundational structure for www.MedicalCharity.org , which is also expected to be launched in 2005. The organization will make it easy for people to learn about various charities supporting specific medical causes. Additionally a new concept in charity will be introduced. Contributions can be directed toward local health food stores, pharmacies and health care professionals to purchase supplements and services for those less fortunate financially. There is a tremendous need for such a program. Despite often being professionally recommended, insurance and government programs seldom reimburse patients requiring these services or nutritional supplements.

Dr. Ivana Vucenik Ph.D. joined the Dept of Medical & Research Technology, University of Maryland School of Medicine in 1990. She is an associate professor and director of the graduate program. She is investigating the effect of IP_6 on cell growth, differentiation, and its interaction with intracellular signal transduction pathways to understand the mechanism(s) underlying this antineoplastic action. She is also studying the antiplatelet and natural killer (NK)-cell enhancing functions of IP_6. Another research project focuses on tumor markers expressed during cancer formation and its usefulness for early diagnosis and screening. Her research has been supported by grants from The American Institute for Cancer Research, Women's Health Research Group at UMB, and the Susan Komen Breast Cancer Foundation.