

SOME OF THE PUBLISHED ARTICLES ON ANTI-CANCER PROPERTIES OF SEAWEEDS/CARRAGEENAN

IMMUNOMODULATION AND ANTITUMOR ACTIVITY OF K-CARRAGEENAN OLIGOSACCHARIDES

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Abstract

The modulation of carrageenan oligosaccharides from *Kappaphycus striatum* on the immune system in S180-bearing mice was investigated. The mice inoculated with S180 cell suspension were treated p.o. with carrageenan oligosaccharides (50, 100 and 200 µg/g) for 14 days. The effects of carrageenan oligosaccharides on transplantable tumors and macrophage phagocytosis, quantitative hemolysis of sheep red blood cells (QHS), lymphocyte proliferation, the activity of natural killer cells (NK), production of interleukin-2 (IL-2) and tumor necrosis factor-α (TNF-α) were studied. Carrageenan oligosaccharides could significantly inhibit the growth of transplantable sarcoma S180 and increase macrophage phagocytosis, the form of antibody secreted by spleen cells, spleen lymphocyte proliferation, NK cells activity, serumal IL-2 and TNF-α level in S180-bearing mice. Considering all these results, it is suggested that carrageenan oligosaccharides exert their antitumor effect by promoting the immune system.

SEAWEED EXTRACT PROTECTS AGAINST HERPES

Carrageenan, a extract of red seaweed, when added to spermicide with nonoxynol-9 has been found to protect again HSV-2. This conclusion was reached following a study with mice conducted by the Population Council located in New York.

Researches said that this combination proved to more effective against HSV-2 infection than Gynol-II or K-Y Plus by improving microbe- killing properties without diluting sperm-killing activity.

Carrageenan is considered a likely addition to products such as spermicide because it is considered safe, stable, inexpensive, easily available and is not absorbed by the body. (Journal of Sexually Transmitted Diseases, Nov. 1999)

Of the products in development, the one farthest along in clinical testing is Carraguard, a three percent carrageenan gel. Two randomized, placebo controlled Phase II expanded safety and acceptability studies have been completed. A total of 165 women were enrolled in Thailand and 400 in South Africa. Women were randomly assigned to Carraguard or placebo, a methyl cellulose gel, and asked to insert their assigned product for a minimum of three times per week. Preliminary findings showed similar rates of HIV/STI and of genital lesions in both groups.

SULFATED POLYSACCHARIDES (CHONDROITIN SULFATE AND CARRAGEENAN) PLUS GLUCOSAMINE SULFATE ARE POTENT INHIBITORS OF HIV

Chondroitin Sulfate - A Fusion Inhibitor

Mark Konlee

An article by DS Newburg et al in the Journal of Nutrition (4) reports that “Human milk glycosaminoglycans inhibit HIV glycoprotein gp120 binding to its host cell CD4 receptor.” Newburg reports that the binding of the gp120 on the membrane of the HIV virus to a target cell is the first step that must happen before HIV can infect a new cell. Any substance that can block the ability of a virus to infect a cell is called a fusion inhibitor which means that the virus is prevented from injecting its genetic material into the cell. Blocking the ability of a virus to infect a cell stop the spread of an infection at its very origin. A fusion inhibitor is to a virus what a mosquito repellent is to a mosquito; it prevent the virus (i.e. mosquito) from making surface contact with the host. Newburg has discovered a natural fusion inhibitor in human milk called chondroitin sulfate.

Newburg et al wrote: “The binding of the HIV envelope glycoprotein, gp 120, to its host cell receptor, CD4, is inhibited in a solid phase assay by a glycosaminoglycan of human milk; this binding is the essential first step in HIV infectivity.” Human milk contains dermatan sulfate, heparin, heparin sulfate, and chondroitin sulfate. Newburg found that when lytic enzymes that were specific for dermatan sulfate, heparin and heparin sulfate were added to human milk, they did not affect the inhibition of gp 120 to bind to the CD4 cells. However, when lytic enzymes were added specific for chondroitin sulfate, the ability to block binding of the HIV glycoprotein (gp 120) to the CD4 cells was lost. Newburg concludes: “This indicates that the ability of human milk to inhibit gp120 binding to CD4 may be attributed to chondroitin sulfate...rather than to other components of human milk.” Newburg then speculates that the human milk glycosaminoglycan (chondroitin sulfate), could limit the rate of vertical transmission of HIV in breast-fed infants of HIV-infected mothers (4).

Since chondroitin sulfate is found in human milk, might it not also be found in cow and goat’s milk? Chondroitin sulfate is found naturally in Shark cartilage and Bovine Trachea cartilage. Today, it is widely available as a dietary supplement in both health food stores and pharmacies and is often used with glucosamine sulfate as a treatment for Arthritis and Rheumatism. Interestingly, an Indian medicine man from Canada told me that he “cured” over 100 cases of arthritis among his fellow Indians by having them drink raw (unpasteurized) cow’s milk that was preheated until it was lukewarm or would dissolve a dab of butter. Could pasteurization of milk

impair the ability of the digestive tract to absorb chondroitin sulfate? On the other hand, absorption of chondroitin sulfate from pasteurized milk might still be occurring. I recall a case about 3 years where a PWA (person with aids) told me he gained 20 lbs by drinking 2 quarts of milk daily. I have read that glucosamine sulfate has a smaller molecular weight than chondroitin sulfate and is 98% absorbed whereas chondroitin sulfate is 13% absorbed(7). (Possibly, chondroitin sulfate's anti-HIV action is primarily located in the gastrointestinal tract).

(Note: Pasteurization of milk is done to prevent transmission of diseases like bovine tuberculosis from cows to people. Consumption of raw milk should be only from a dairy cow certified by a veterinarian to be free of any transmissible disease. Two states, California and I believe Vermont allow for the public sale of Certified Organic Raw Milk.) Glucosamine 6-sulfate found to have significant anti-HIV activity. Basgasra et al of the Jefferson Medical College in Philadelphia, PA found that sulfated polysaccharides and one sulfated monosaccharide, glucosamine 6-sulfate, have significant anti-HIV activity (1). The authors discussed previous research that found that 4 sulfated polysaccharides: dextran sulfate, pentosane polysulfate, chondroitin sulfate and heparin sulfate, had anti-HIV activity. Basgasra tested these using 4 different assays to measure anti-HIV activity and concluded that "only sulfated polysaccharides and one sulfated monosaccharide, glucosamine 6-sulfate, have significant anti HIV-1 activity."

CARRAGEENAN (derived from red seaweed)

Carrageenan is a substance with natural gelling and thickening properties that is used as a food additive in ice cream, sauces and salad dressings. It is found naturally in Irish Moss and in several other species of red seaweed. Carrageenan, derived from red seaweed is processed to remove the marine flavor and is listed by the FDA on its GRAS list (generally recognized as safe).

R Pratt-Pearce and DM Phillips found that sulfated polysaccharides inhibited lymphocyte to epithelial transmission of HIV (2). The authors of this article suggested that iota carrageenan be used as a vaginal microbicide to prevent HIV transmission. They wrote:

"In the present in vitro study, evidence is presented that a number of sulfated polysaccharides, including carrageenan, dextran sulfate, heparin, fucoidal and pentosan polysulfate, are capable of blocking (HIV) infection by mechanisms other than adhesion at concentrations of a thousand times lower than the dosages that are needed to block cell adhesion. One of these compounds, iota carrageenan, is capable not only of blocking infection of epithelia at concentrations of 1-2 micrograms, but of blocking adhesion to a far greater extent than the other sulfated polysaccharides tested."

The authors suggested that carrageenan be tested as a vaginal microbicide to prevent HIV transmission. 12th Int'l AIDS Conference: Abstract no 33155 by David Philips et al reported on various concentrations of carrageenan placed in vagina of mice and reported that "Formulations of carrageenan may be effective in blocking infection by HSV-2 without affecting fertility. Carrageenan based N9 spermicides may be more efficacious than existing glycerol based formulations in preventing infection by herpes simplex virus and possibly other

enveloped viruses.” (5) Another abstract at the conference found that a 2% formulation of the sulfated polysaccharide carrageenan “protected all the animals from HSV-2 infection.” (6)

Several abstracts indicated that in mice, carrageenan suppressed macrophage activity. This, however, has not been demonstrated in humans and in the experiments with mice, the carrageenan was injected which could elicit a completely different immune response that when the carrageenan is orally ingested and goes through the digestive process. The question of whether oral use of carrageenan in humans might suppress macrophage activity is not resolved and needs to be studied further.

Nothing has shown up in scientific literature that indicates the other sulfated polysaccharides, chondroitin and glucosamine, have any effect one way or the other, on macrophage activity. Shark cartilage, used to treat cancer and arthritis, contains chondroitin sulfate. However, the effects of various types of sulfated polysaccharides on natural killer cell and CD8 cytotoxic lymphocyte activity needs to be studied and weighed along with its anti-viral effects to get a complete picture of its therapeutic value and its effects on immune function. In a further contradiction of carrageenan’s effects on the immune system, a Material Safety Data Sheet from FMC corporation indicated that in animal studies, small amounts of carrageenan in rats suppressed immune function while larger doses stimulated it. (2)

Why study the anti-viral and immunological effects of carrageenan, agar and irish moss if chondroitin and glucosamine sulfate prove safe and effective for HIV and other lipid envelope viruses? The answer is to expand treatment options to determine the most effective, yet safe forms of sulfated polysaccharides available, and if any of these forms might actually totally eradicate HIV, HHV-6A and other lipid envelope viruses from the body.

1. Fuji Y et al; Microbiol Immunol 1990;34(6):533

2. J. Reticuloendothelial Soc. 28:213, 1980

3. “Glucosamine Sulfate and Chondroitin Sulfate,” by Rita Elkins M.A, M.H., Woodland Publishing Inc., Pleasant Grove, UT.

ARE SULFATED POLYSACCHARIDES IN SEA VEGETABLES ABSORBED?

HOW EFFECTIVE WILL THEY BE AS ANTI-VIRALS FOR HIV AND OTHER VIRUSES?

One question that was not addressed at the 12th Int’l AIDS Conference is if the oral consumption of carrageenan or other forms of sulfated polysaccharides found in agar agar, irish moss and other sea vegetables would be absorbed and then lower the HIV plasma viral load. This is an important question to be answered considering the low cost and availability of these products and the critical need to find an effective low-cost treatment for poor people in third world countries.

Sulfated polysaccharides exist in red seaweed, Irish moss, agar agar and other sea vegetables and plants. Could sulfated polysaccharides exist in wakame (used in Miso soup)? Might this

partially explain the success of traditional macrobiotic diets in stopping HIV progression to AIDS? Macrobiotic diets usually include a generous daily portion of vegetables from the sea.

References:

1. Anti-HIV virus type 1 activity of sulfated monosaccharides: comparison with sulfated polysaccharides and other polyions, Basgasra O et al; J. Inject Dis. 1991 Dec; 164(6):1082-90
2. Sulfated polysaccharides inhibit lymphocyte to epithelial transmission of HIV-1, Pearce-Pratt R et al, Biol Reprod. 1996 Jan; 54(1):173-82
3. Interaction of HIV-1 Tat protein with heparin. Role of the backbone structure, sulfation, and size. Rusnati M et al; J. Biol Chem. 1997 Apr 25; 272 (17):11313-20
4. Human milk glycoaminoglycans inhibit HIV glycoprotein gp 120 binding to its host CD4 receptor, Newburg DS et al, J. Nutr. 1995 Mar; 125 (3):419-24
5. Carrageenan based formulations for preventing infection by enveloped viruses, David Phillips et al, Population Council, 1230 York ave, New York, NY XII Int'l AIDS Conference, Abstract no 33155.
6. Abstract No 33143, by David Phillips et al. 12th Int'l AIDS Conference.
7. "Glucosamine Sulfate and Chondroitin Sulfate," by Rita Elkins M.A, M.H., Woodland Publishing Inc., Pleasant Grove, UT.

SULFATED POLYSACCHARIDES INHIBIT HIV, CMV, HERPES AND OTHER LIPID ENVELOPE VIRUSES.

WILL THEY ALSO INHIBIT HHV-6?

Researchers Baba M et al from Belgium reported as long ago as November, 1988, that "Sulfated polysaccharides are potent and selective inhibitors of various enveloped viruses, including herpes simplex virus, cytomegalovirus, vesicular stomatitis virus, and human immunodeficiency virus." (1)

The researchers reported that sulfated polysaccharides (dextran sulfate...fucoidan and carrageenans) proved to be potent inhibitors for herpes simplex virus, human cytomegalovirus, vesicular stomatitis virus, Sindbis virus, and HIV, but not inhibitory to adenovirus, poliiovirus and parainfluenza virus. They wrote that "with the exception of parainfluenza virus, enveloped viruses are specifically susceptible to the inhibitory activity of sulfated polysaccharides."

Another seaweed, a red algae "Schizmenia pacifica" was found by Nakashima et al to be a reverse transcriptase inhibitor against HIV. These researchers also reported that chondroitin sulfate had reverse transcriptase inhibitory activity (2).

AGAR FOUND TO HAVE SULFATED POLYSACCHARIDES

Another plant from the sea, Agar Agar, was found to have sulfated polysaccharides (agaropectin)(3). Agar is often added to processed foods for its gelling properties. However, no published research has been found to determine if the sulfated polysaccharides in Agar will inhibit lipid envelope viruses. Agar as well as other species of red seaweed need further research to determine their full potential anti-viral properties.

Other red seaweeds where sulfated polysaccharides were found are *Gracilaria dominguis* (4), *Nothogenia fastigiata* (5) and *Grateloupia indica* (6). *Chondrus crispus* (Irish Moss) was found to contain kappa-carrageenan as the major component with 1-carrageenan and sulfated galactans as minor components (7). In August, 1986, in the publication "Shigaku," Natsuno et al reported "a potent inhibitor of bacterial growth from a seaweed, *Chondrus crispus*."

1. Baba M et al, Rega Institute for Medical Research at Katholieke Universiteit Leuven; *Antimicrob Agents Chemother* 1988 Nov;32(11):1742-5
2. "Sulfated Polysaccharides extracted from sea algae," by Nakashima H et al; *Antimicrob Agents Chemther* 1987 Oct; 31(10):1524-8
3. Rochette J et al; published in *Electrophoresis* 1989 Dec;10(12):853-6.
4. "Isolation and characterization of an antitumor active agar-type polysaccharide of *Gracilaria dominguis*," by Fernandez LE et al. *Carbohydr Res* 1989 Jul 1;190(1):77-83.
5. "Kolender AA et al; *Carbohydr Res* 1997 Oct 28;304(1):53-60
6. Sen AK Sr et al; *Int J Biol Macromol* 1994 Oct;16(5):279-80
7. "Heterogeneity of carrageenans from *Chondrus crispus*," by Matsuhiro B and Urzua CC. Source: *Phytochemistry* 1992 Feb;31(2):531-4.

SILICA AND/OR CARRAGEENAN BLOCK IgG SUPPRESSION OF NATURAL KILLER CELL ACTIVITY IN NUDE MICE

An interesting study by Fuji Y et al at the Nagoya Univ. School of Medicine found that IgG antibodies in-vivo (in a live host) diminished the NK cell activity of nude mouse spleen cells and that preadministration with silica or carrageenan blocked the effects of IgG in suppressing NK cell activity. (1). My interpretation of this article suggests that silica or carrageenan may block TH2 cytokine stimulated antibody (IgG) activity that suppresses the TH1 cytokine Natural killer cell and CD8 cytotoxic lymphocyte activity (CTL) in the presence of complement.

This suggests that silica (bioactive silicon) or carrageenan, by suppressing TH2 antibody activity, might help promote NK and CTL immune responses that would be beneficial in conditions like AIDS, CFIDS and even cancer. Bio-Sil, a biologically active form of liquid silicon manufactured by

Jarrow Formulas is sold in health food stores. The herb "horsetail" or "shavegrass" is a natural source high in silicon. Other herbs that contain silicon are black walnut, burdock, cornsilk, gentian, ginseng, nettle, oatstraw, peppermint, rosehips and stevia, a natural sweetener. The use of these herbs as a natural source of silica might benefit persons affected by AIDS, CFIDS, Gulf War Syndrome and other conditions if they ultimately prove to help shift the cytokine profile from TH2 to TH1 thus helping to improve CD8 cytotoxic lymphocyte and NK cell activity.

LOW COST TREATMENTS FOR CANCER AND AIDS ARE KEPT IN LOW PROFILE

In the war against cancer and chronic intracellular infections, the dietary supplement industry has discovered the importance of the Natural Killer cells. An increasing number of products are coming on the market that claim to increase NK function. MGN3 by Lane Labs is the most recent challenger to Enzymatic Therapies IP6. NK911 was the first product we reported in the fall of 1997 that was backed by studies indicating its effectiveness in improving NK function. Naltrexone has a long history of effectiveness in improving NK function but requires a prescription that is sometimes difficult to obtain. Like DNCB, its low cost and low profit also keep it in a low profile.

Most people with chronic illness do not have unlimited funds to just keep adding on to their program every new promising product that comes along. There are no marketing forces to finance and promote low cost treatments for AIDS, let alone cancer or any other disease. To develop outright cures for any illness would reduce sales volume and profits. The stockholder's bottom line would be adversely impacted. There clearly are a lack of leaders at all levels of society who want to step into Mother Teresa's shoes. Materialism corrupts mankind and wastes limited resources while looming like a dark cloud on the horizon is the spectacle of a world ridden by interest-bearing debts and a collapsing international monetary system.

Of 30,000 million infected by HIV and probably HHV-6(a) worldwide, fewer than 5% can afford or have governments that can afford to buy them the most promising of the pharmaceutical drugs now available. This means that for 28 million people in poorer underdeveloped countries, these are options beyond reach. As the FDA approves more and yet more drugs to treat AIDS, the pharmaceuticals companies are battling over 5% of the market. What the world needs is not more \$2000 a month treatments for AIDS, but more \$50 to \$100 a month treatments that work just as well.

SUPPRESSION OF CYTOTOXIC T LYMPHOCYTES BY CARRAGEENAN-ACTIVATED MACROPHAGE-LIKE CELLS¹

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Abstract

In the presence of 100 µg/ml of carrageenans (CAR), B6D2F₁ responder spleen cells failed to generate anti-parent or anti-allogeneic cytotoxic T lymphocytes *in vitro*, but instead generated suppressor cells. Cultured CAR-treated cells added to mixtures of B6D2F₁ anti-B6 or B6D2F₁ anti-C3H cytotoxic effectors (induced *in vitro*) and the appropriate ⁵¹Cr-labeled lymphoma targets reduced or abolished cytolysis (measured as ⁵¹Cr release) depending on the ratio of suppressor to effector cells. Cultured spleen cells not exposed to CAR failed to inhibit both types of cytotoxicity.

Presuppressor cells were associated with a splenic subpopulation independent of the thymus (i.e., present in spleens of athymic nude mice), were moderately adherent to Sephadex G-10 columns, but were not phagocytic or "sticky" to carbonyl iron particles. Activation of such cells by CAR was not prevented by *in vitro* exposure to 2000 rads of γ-rays before culture, nor facilitated by antigenic stimulation. The matured suppressor cells remained radioresistant and became strongly adherent to Sephadex G-10. The suppressors lacked surface Thy-1 alloantigen detectable by antibody and rabbit complement. Suppressor cell activity was not restricted by the immunologic specificity and major histocompatibility type of effectors.

It would thus appear that CAR induced the transition from the presuppressor to the suppressor state of a macrophage-like splenic subpopulation via maturation, differentiation, or cell injury. Cells of this type, capable of inhibiting the effector arm of cell-mediated responses, may well contribute to the regulation of natural and induced cytotoxic cell interactions.

ORGANIC SEA GREENS - GIFTS OF HEALING FROM THE SEA

by Linda Page, N.D., Ph.D.

Author of *Healthy Healing - A Guide To Self-Healing For Everyone*

I believe sea greens (otherwise known as seaweed, sea vegetables and algae) are one of God's greatest gifts to us. Grown by Mother Ocean, the birthplace and primary nourisher of life on Earth, sea greens offer us amazing health benefits. They are the most nutrition-dense plants on the planet. Ounce for ounce, along with herbs, they are higher in vitamins and minerals than any other food. I eat delicious organic sea greens every day.

Sea greens are one of nature's richest sources of vegetable protein; they provide full-spectrum concentrations of carotenes, chlorophyll, enzymes, amino acids and fiber. The distinctive salty taste is not just "salt," but a balanced, chelated combination of sodium, potassium, calcium, magnesium, phosphorus, iron and trace minerals. They contain 10 to 20 times the minerals of land plants, and even beyond their mineral quantities, their mineral balance is a natural stabilizer for building sound nerve structure and good metabolism.

Sea greens are rich in fiber and packed with vitamins, with measurable amounts of vitamins K, A, D, B, E and C, and beta carotene. Sea greens are almost the only non-animal source of Vitamin B-12 necessary for cell development and nerve function. They are full of amino acids, contain up to 20% protein, and have enzymes and essential fatty acids that rejuvenate us. Sea greens nourish an underactive thyroid and normalize adrenal functions which results in an increased libido.

I've been teaching about the health benefits of sea greens for years! They are an excellent weapon against heart disease, helping to dissolve fatty deposits in the cardiovascular system that lead to heart disease, and relieving tension in blood vessels caused by over-consumption of salty foods. Japanese studies from the 1960s show extracts from sea greens control high blood pressure and atherosclerosis even in animals fed a high cholesterol diet. The same studies found sea greens also lowered blood pressure in people!

Sea greens have antiviral, antimicrobial, and antifungal activity. They're anti-inflammatory too, offering a one-two punch against many infections. Immune-compromised diseases like chronic fatigue, HIV infection, arthritis and allergies respond to sea plant treatment. Sea greens are at their best in just this type of role--as balancers for body chemistry which is regularly imbalanced in immune-compromised disease. The chemical composition of sea greens is so close to human plasma, that perhaps the greatest benefit from sea greens is that they help normalize our bodies from the effects of a modern diet. They strengthen us against disease, and reduce excess stores of fluid and fat. Many people notice a rapid difference in their weight, and an increase in their calorie burning when they eat sea greens regularly.

Modern science is validating many of the traditional benefits of sea plants, especially their algin, the component thought to be responsible for the success of seaweeds in the treatment of obesity, asthma, atherosclerosis and blood purification. Studies done at McGill University reveal that algin binds to chemical toxins and pollutants in the intestinal tract, allowing them to be safely eliminated before they can poison the body.

Sea greens can protect us from a wide range of toxic elements in the environment, including heavy metals (most dental fillings still contain them) and radiation by-products, converting them into harmless salts that we can eliminate. The natural iodine in sea greens can reduce by almost 80% the radioactive iodine-131 absorbed by the thyroid and is a key to controlling and preventing gland disorders like breast and uterine fibroids, prostate inflammation, adrenal exhaustion, and toxic liver and kidney states. Preventive measures may be taken against

iodine deficiency problems or disease risk by adding just 2 tablespoons of chopped, dried sea greens to your daily diet.

Studies from the Harvard School of Public Health show that eating kelp as about 5% of your diet inhibits cancer growth and even causes remission of active tumors. Sea greens contain powerful antioxidant and anti-cancer properties, working to stop the proliferation of cancer cells. Some experts consider them more potent than the drugs now used to treat breast and prostate cancer, especially as interceptive measures. The latest research from Japan reveals a seaweed extract from kombu, fucoidan, actually causes cancer cells to self-destruct (a process technically referred to as cancer cell apoptosis). Stomach cancer, colon cancer and leukemia all responded positively to fucoidan treatment in animal tests and in vitro (test tube) studies.

Sea greens have high magnesium, essential for the absorption of calcium. Magnesium stimulates production of calcitonin, the hormone which increases calcium in the bones. Sea greens are a good source of natural vitamin D, too, essential for calcium absorption, bone health and muscle function.

SEAWEED EXTRACT PROTECTS AGAINST CERVICAL CANCER

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Algae compound surprisingly effective at preventing cancer-causing viral infection.

Just a tiny amount of a common food additive has been found, in lab tests, to guard against the virus linked to cervical cancer.