Plant sterols and sterolins: Potential immune system modulators

Sterols are plant fats found in all plant-based foods. Sterols, including cholesterol, are in the same large classification family of steroids but they do not have the negative effects that often are associated with steroids. Sterolins are glucosides, which are molecular structures joined to the sterol. Sterolin is easily destroyed, and without it, the sterol does not have the same immune-enhancing benefits. In nature, plants never contain sterols only. The sterols are always associated with their glucoside sterolin. The original research on sterols and sterolins was based on an extract of the African Hypoxis plant or "African Potato." Its nomenclature derived because of the potato-like appearance of the Hypoxis plant. Because of the presence of other potentially harmful substances contained within the Hypoxis plant, other plants were investigated as sources for the sterols and sterolins used in supplementation.

Wheat, for instance, contains about 4,200 milligrams of plant sterols per 100 grams, while wheat flour contains only about 52 milligrams of total plant sterols per 100 grams! The removed bran contains about 4,500 milligrams of total plant sterols per 100 grams and the unrefined oil about 2,600 milligrams per 100 grams. Crude plant oils are a relatively rich source of phytosterols and their glucosides, but most of these are removed during refining. While soybeans contain about 160 milligrams of total plant sterols per 100 grams, the crude oil contains approximately 350 milligrams. This is reduced to 220 milligrams when the oil is refined and is further reduced during hydrogenation. This applies to all plant oils.

In order to consume 100 milligrams of plant sterols, however, one would have to eat 500 to 700 grams of fresh vegetables and fruit or about 200 grams of flour products (without additives). This amount has to be doubled for a normal dietary supply due to the fact that sterols and sterolins are tightly bound to plant fiber and therefore are not completely absorbed. When processed food is eaten or when one is under stress, the attenuated rate of sterolin/sterol absorption is more acute. Slimming diets, ill health and old age also seriously reduce the intake of sterols and sterolins.

Sterols and sterolins seem to illicit immune regulating effects. Before we discuss this let's take a closer look at the immune system.

The immune response has two ways of dealing with foreign pathogens. The B-lymphocytes synthesize specific antibodies called immunoglobulins. This is known as humoral immunity. The other system involves T-lymphocytes, which regulate the synthesis of antibodies as well as direct killer cell activity and the inflammatory response of delayed type hypersensitivity. This system is known as cell-mediated immunity. The T-cells are further divided into helper lymphocytes (Th) and cytotoxic cells (Tc), also known as suppressor cells. When the T-cells encounter a foreign pathogen (antigen) they further secrete a number of communication molecules called lymphokines, cytokines, interleukins or interferons. These factors further elaborate and direct the immune response to a specific antigen. The whole process is a symphony of many co-factors, which are orchestrated into a sophisticated immune response. The T-helper cells are directly involved in assisting B-cells as well as coordinating their own cell-specific defense. The T-helper cells are further divided into two distinct lines of defense. The Th1 cells promote the cell-mediated line of defense and inhibit the other line known as Th2 cells, which regulate the humoral defense. The Th2 cell lines control the B-cells and inhibit the cell-mediated response of the Th1 lymphocytes. A careful balance between these two functions is

thus achieved. When one line predominates, there is the opportunity for immune dysregulation to occur, resulting in either a hyper-immune response causing an autoimmune disease or a hypo-immune response resulting in an uncontrollable infection such as AIDS or tuberculosis. The Th1 helper cells secrete lymphokines such as interleukin-2 and gamma interferon. Th2 helper cells secrete pro-inflammatory lymphokines such as interleukin-6, interleukin-4 and interleukin-10. Interleukin-1 appears to be released in response to a specific injury and acts as an inflammatory mediator. Interleukin may be over-expressed in diseases such as rheumatoid arthritis and osteoarthritis. Interleukin-1 deficiency is associated with metastatic tumors, nutritional deficiencies and certain autoimmune diseases. Interleukin-6 is associated with pro-inflammatory responses as well as mediating the proliferation and maturation of T-cells. High levels of interleukin-6 have been associated with a variety of autoimmune conditions such as rheumatoid arthritis, Sjogren's syndrome, multiple myelomas and some cancers such as cervical and bladder cancer. Interleukin-2 is a growth factor for T-cell maturation as well as an inducer of T-cell cytotoxicity and natural killer cell activity. An interleukin-2 deficiency would cripple the cell-mediated immune response and its stimulation would enhance the overall efficacy of the immune system. Immune dysregulation occurs when the two sides of the immune response become imbalanced.

Stress and our body chemistry

The body has developed mechanisms to protect it from the damaging effects of stress. The "fight-or-flight" response is one way the body deals with extreme situations of stress. Upon realizing we are in danger, the brain sounds an alarm, telling our adrenal glands to secrete adrenaline and cortisol, which mobilizes the body to fight or run. This response is supposed to be a short-lived reaction yet today most of us are in and out of this state continually. As a result, our immune system becomes imbalanced, sending out too many inflammatory cytokines. Our adrenal glands become exhausted, weakening several body systems, especially the cardiovascular and endocrine systems. What mechanism in the body occurs when we are under constant stress that causes disease?

When we are exposed to stressors our adrenal glands secrete the stress hormone cortisol, causing a corresponding drop in our anti-aging and immune enhancing hormone dehydroepiandrosterone (DHEA). A tremendous body of research has shown that when cortisol goes up, DHEA drops and when DHEA is normal, cortisol also normalizes. Low DHEA levels are seen in those that are immune compromised, have arteriosclerosis (hardening of the arteries), diabetes and lupus.

Cortisol helps the body maintain homeostasis in the face of stressors counteracts inflammatory and allergic reactions, and controls the metabolism of protein and carbohydrates. Cortisol is a very misunderstood hormone. Balance is the key. In naturally low doses it stimulates the immune system and in high doses, as prescribed in synthetic drug form, it can be immune suppressing. Remember that cortisol plays a role in counteracting inflammatory responses in the immune system and when cortisol is not available because the adrenal glands have become exhausted from too much stress, inflammation is allowed to continue unchecked. Conversely, too much cortisol and you have immune suppression.

The immune system also responds to stressors by causing certain immune cells to secrete the pro-inflammatory cytokines, Interleukin-1 (IL-1) and Interleukin-6 (IL-6). These cytokines are both involved in inflammation and IL-6 in particular is thought to worsen the symptoms of autoimmune diseases and fibromyalgia. Interleukin-6 has been found to act as a growth factor in several tumors and some viruses also use IL-6 to replicate. Interleukin-6 also causes calcium to be released from bone, promoting osteoporosis. We must control the release of these cytokines if

we want to enhance immunity and reduce degenerative diseases.

In the presence of stressors the immune system and endocrine system work as an integrated circuit. Deficiencies in the immune system and abnormalities in the cross talk with the endocrine system can influence the susceptibility of developing chronic inflammatory disease, autoimmune disease like lupus, rheumatoid arthritis and osteoporosis, reduce the ability to fight infections and it can cause muscle atrophy, rapid aging, poor antibody production against vaccines and more. Modulating or keeping cortisol levels in balance through a healthy diet, nutritional supplements and stress reduction are keys to disease prevention.

Mother Nature's cortisol balancer

Endurance athletes often are studied because the effects of excessive exercise mimic other stressful events. Excessive physical stress causes tissue damage and in response promotes the release of cortisol and pro-inflammatory cytokines, especially Interleukin-6. DHEA and suppressed immunity also are seen in athletes that exercise to excess. Professor Patrick Bouic and his research team have shown that a plant nutrient called sterols and sterolins effectively modulates cortisol and controls Interleukin-6 and naturally increases DHEA. In a double-blind, placebo-controlled study published in the *International Journal of Sports Medicine* a group of 20 athletes were evaluated pre- and post-marathon run. Post-marathon results showed that the group treated with sterols and sterolins displayed a significant reduction in Interleukin-6 compared to the placebo group. A profound effect was observed in the balance between cortisol and DHEA levels in the sterol and sterolin-treated group. Cortisol increased as expected in the non-treatment group, causing immune suppression; it dropped in the group taking the sterols and sterolins. The cortisol decrease was accompanied by an increase in DHEA that was statistically significant.

Antioxidant nutrients, including vitamins A, C, E, B6, B3 and selenium, zinc, magnesium, coenzyme Q10, N-Acetyl-L-Cysteine, alpha lipoic acid, essential fatty acids and an excellent diet rich in lean protein, complex carbohydrates with adequate amounts of organic fruits and vegetables should also be adopted to provide a powerful nutritional defense against the negative effects of stress. The mind and body is one unit, interrelated and highly complex. Though it may take a while for scientists to truly understand the intricacies of how stress affects immunity and the aging process, today we know that having a positive attitude, a loving family, friends and effective stress-coping strategies enhance our immune system and give us a few extra years.

Sterols and sterolins in clinical research

A randomized placebo-controlled trial of the efficacy of beta-sitosterol and its glucoside as adjuvants in the treatment of pulmonary tuberculosis.

Author: P.R. Donald; J.H. Lamprecht; M. Freestone; C.F.Albrecht; P.J.D. Bouic; D. Kotze; P.P. van Jaarsveld Source: International Journal of Tuberculosis and Lung Disease, vol. 1 (5), pp. 518-522, July 1997

This is a double-blind study of 43 persons positively infected with pulmonary tuberculosis receiving conventional multi-antibiotic treatment to ascertain if the addition of a plant sterol/sterolin mixture could improve the clinical outcome. The study took place over 6 months and the patients were closely monitored with a variety of lab and radiographic tests. The groups receiving the sterol/sterolin mixture showed a significant weight gain over the placebo group. As well, the treatment group showed a significant increase in lymphocytes and eosinophils. The increase in lymphocytes is consistent with previous experiments indicating a T-cell

proliferative effect with the oral intake of phytosterols. The increase in eosinophils is difficult to explain, since no previous allergic response has been attributable to the ingestion of the phytosterols. However, other data indicate there may be a relationship between the rise of CD4 lymphocytes and eosinophils. Plant sterols/sterolins have been demonstrated elsewhere to selectively increase CD4 lymphocyte counts. Other lab parameters remained the same between the two groups including hemoglobin, hematocrit, neutrophil count, serum globulin, creatinine, and urea. This preliminary study indicates that plant sterols and sterolins may have a positive role to play in the complementary treatment of immunocompromised patients.

Randomized, placebo-controlled, double blind clinical trial of b-sitosterol in patients with benign prostatic hyperplasia

Author: R.R. Berges; J. Windeler; H.J. Trampisch; T.H. Senge and the b-sitosterol study group. Source: Lancet, vol. 345, no. 8964, pp. 1529-32, June 1995

This is a randomized, double blind, placebo-controlled, multi-center study of 200 men with BPH (benign prostatic hyperplasia) treated with the phytosterol, B-sitosterol. Two hundred men were selected and followed for 6 months using a variety of lab tests, and subjective and objective symptom indicators for BPH. Half the group received the active treatment, 20 mg B-sitosterol three times daily and the other half received the placebo. The results indicate that the group treated with B-sitosterol improved in both subjective symptoms of BPH and the objective measurement of improved urine flow. These results occurred independent of a reduction in actual prostate size. Only minor side effects were observed with the phytosterol treatment group compared to the more toxic side effects associated with the 5-alpha-reductase inhibitor drugs such as finasteride. No mechanism for the effects of B-sitosterol on the prostate has been elucidated as yet. This study indicates that traditional herbal treatment of BPH with saw palmetto; pygeum africanus and pumpkin seeds may be attributable to the phytosterol content of these herbs. A German herbal preparation sold for the last 20 years under the trade name Harzol for the treatment of BPH contains a mixture of phytosterols including B-sitosterol.

A pilot study of the clinical effects of a mixture of beta-sitosterol and beta-sitosterol glucoside in active rheumatoid arthritis (RA).

Authors: Ingrid Louw, Anne Halland, Panaroma Hospital, Patrick Jacques Desire Bouic, University of Stellenbosch, Marga Freestone, Essential Sterolin Products (Pty) Ltd, Johan Lamprecht, University of Stellenbosch

Introduction: The mixture of Beta-sitosterol (BSS) and Beta-sitosterol glucoside (BSSG) has demonstrated anti-inflammatory activities in vitro, inhibiting the secretion of IL6 and TNF-alpha from activated monocytes. Both factors are implicated in the pathogenesis of RA.

Objective: Could the BSS: BSSG mixture result in the improvement of active RA as assessed by ACR 20% response criteria?

Methods: After a two-week placebo run-in phase, patients with active RA were randomized to receive either 20mg BSS/0.2mg BSSG capsules tid or placebo (225mg carrier) tid for 24 weeks. Mean demographics of the patient groups were similar. All patients had active RA as defined by ACR criteria. Stable DMARD doses were required for 3 months prior to the start and for the duration of the study. No new DMARD therapy could be initiated during the study. Patient response was assessed in terms of ACR response criteria (>20% improvement). Significant changes between active and placebo groups were calculated with the Kruskal-Wallis 2-sample test. Changes within

a group relative to baseline were calculated with the Wilcoxon rank test.

Results: 18 Patients were enrolled (8 on actives and 10 on placebo). In the active group, statistically significant changes were measurable in the mean tender joint count (85% ACR response); patient's assessment of pain (28% response); patient's global assessment of disease activity (33% response); physician's global assessment of pain (47%) and the MHAQ decreased (47% response). The ESR also decreased significantly (56% response). The placebo group had no significant improvement in the ACR 20% improvement criteria. At 24 weeks, significant differences between groups with regards to tender joint count, MHAQ, physician's global assessment and patient's assessment of disease activity were demonstrated. The BSS: BSSG mixture was well tolerated and no serious adverse events were recorded.

The effects of b-sitosterol (BSS) and b-sitosterol glucoside (BSSG) mixture on selected immune parameters of marathon runners: inhibition of post marathon immune suppression and inflammation.

Author: P.J.D. Bouic; P.P. van Jaarsveld; A. Clark; J.H. Lamprecht; M. Freestone and R.W. Liebenberg Source: International Journal of Sports Medicine

A double blind study was performed on marathon runners to see if the addition of a sterol/sterolin mixture would prevent the immune suppression and inflammatory reaction characteristic to high intensity athletics. Twenty marathon runners were recruited to take part in the trial and blood draws and medical histories were taken 4 weeks prior to the marathon event and three days after. Half the group received a placebo and the other half received a 100:1 mixture of sterols/sterolins. The RBC count went down significantly for the placebo group but remained the same for the treatment group. Neutrophils rose significantly for the treatment group, indicating infection, but remained constant in the treatment group. The lymphocyte count went down for the placebo group, specifically the CD3, CD4, and CD8 subsets. The treatment group actually experienced a significant rise for the CD3 and CD4 lymphocyte subsets. Interleukin 6 levels, which indicate an inflammatory reaction, went up for the placebo group, but down in the treatment group. As well, the cortisol levels, which indicate stress levels and degree of immunosuppression, were significantly elevated for the placebo group, but remained constant in the treatment group. The treatment group showed an increase in DHEA levels and a decrease in the cortisol/DHEA ratio, indicating that the sterol/sterolin mixture was helping to buffer the negative side effects of the stress response. The results of this experiment clearly show that taking a sterol/sterolin mixture prior to a highly stressful physical event protected the treatment group from the immunosuppression typically exhibited by the placebo group. As well, the sterol/sterolin mixture protected against the excessive inflammatory response typical of anyone running a marathon. Thirdly, the sterol/sterolin mixture buffered the excessive release of cortisol with its immunosuppressive effects. As well, the sterol/sterolin mixture raised DHEA levels and lowered the cortisol/DHEA ratio, indicating a more adaptive response to stress. These results indicate that sterols/sterolins are adaptogenic in that they modulate the immune and stress response. This makes them extremely valuable adjuncts to the prevention and treatment of a wide range of stress-mediated disorders, as well as immune dysregulation and inflammatory diseases.

Addison's disease, Colitis, Crohn's Disease, Type I Diabetes, Grave's Disease, Hashimoto's Thyroiditis, Lupus, Myasthenia Gravis, Polymyalgia rheumatica, Rheumatoid Arthritis, Scleroderma, and Sjogren's syndrome are autoimmune conditions that could benefit from sterol/sterolin supplementation.

Who should avoid sterol/sterolin supplementation?

Recipients of foreign organs and tissues, including bone marrow and corneal transplants, are cautioned not to take any immune regulating nutritional supplements. Therefore, sterols and sterolins are NOT recommended for transplant patients. People with synthetic replacement/reconstruction will not be affected, such as in hip replacement, knee replacement, breast reconstruction and pacemaker implant.

People with multiple sclerosis should take plant sterols and sterolins only under the guidance of their health care practitioner.

Diabetics should monitor their blood sugar closely as many have experienced a reduction in insulin requirements. They should start with one capsule daily to ensure a gradual increase in sterols and sterolins.

What is the difference between sterol/sterolin supplements and herbs that boost immune response, such as echinacea?

The key difference between echinacea and sterol/sterolin supplements is that echinacea only stimulates the immune system, while sterol/sterolin balances it. Echinacea is not recommended for prolonged use, or for people with autoimmune conditions. Sterols and sterolins allow the immune system to regulate itself: “upregulating” or boosting an underactive response and “downregulating” an overactive one.

Introducing Moducare

Dr. Hoffman is proud to announce that Moducare, a patented unique blend of sterols and sterolins, is available in his dispensary. Moducare contains only the isolated molecules of the sterols and sterolins, which have been extracted from pine trees (Pinus Maritima and Pinus Pinaster). What do you do if you have a pine allergy? There is none of the original plant in the final product. If you looked at these plant fat molecules in a laboratory, you would not be able to tell if they had been extracted from oranges, peas, almonds, etc. If you are still concerned, you can always start slowly with one-half or one capsule per day.

Moducare should be taken on an empty stomach—one half hour before or two hours after a meal for maximum absorption. However it can be taken with fruits and vegetables, nuts and seeds.

The important thing is to remember is to take it away from cholesterol (animal fat), including all meat, dairy, eggs, seafood, etc. Cholesterol has a very similar molecular structure and the two compounds “compete” for absorption. You also can take Moducare with beverages, as long as they contain no cholesterol.

Moducare is the only formula that offers sterols and sterolins in the correct ratio of 100:1, which has been shown to balance and improve immune system functioning. It is recommended as a daily supplement for immune support, as well as part of a targeted program to address autoimmune diseases, under the guidance of a medical doctor.

Dosage information

Adults: 3 capsules daily, usually one in the morning, one in the afternoon, and one in the evening, taken on an empty stomach for maximum absorption. Children: 1 capsule per day for children younger than 5; 2 per day for children between 5 and 12; and children older than 12 can take the adult dose. For very young children who are unable to swallow a capsule, the capsule can be opened and the contents mixed

with applesauce or other fruit/vegetable puree.

Loading phase: When first starting to supplement with Moducare, it is often a good idea (except where contraindicated) to double the daily requirement for the first week or so. This allows the body to build up its reserves as quickly as possible.

References

1. P.R. Donald; J.H. Lamprecht; M. Freestone; C.F.Albrecht; P.J.D. Bouic; D. Kotze; P.P. van Jaarsveld, A randomized placebo-controlled trial of the efficacy of beta-sitosterol and its glucoside as adjuvants in the treatment of pulmonary tuberculosis: International Journal of Tuberculosis and Lung Disease, vol. 1 (5), pp. 518-522, July 1997

2. R.R. Berges; J. Windeler; H.J. Trampisch; T.H. Senge and the b-sitosterol study group, Randomized, placebo-controlled, double-blind clinical trial of B-sitosterol in patients with benign prostatic hyperplasia: Lancet, vol. 345, no. 8964, pp. 1529-32, June 1995

3. P.J.D. Bouic; P.P. van Jaarsveld; A. Clark; J.H. Lamprecht; M. Freestone and R.W. Liebenberg, The effects of B-sitosterol (BSS) and B-sitosterol glucoside (BSSG) mixture on selected immune parameters of marathon runner: Inhibition of post marathon immune suppression and inflammation; International Journal of Sports Medicine, vol. 234, no. 5636, pp.1221-31, May 1997.

4. Dreher, Henry: The Immune Power Personality, Penguin Books USA Inc., New York, 1995.

5. Thibodeau/Patton: The Human Body in Health and Disease, Mosby Publishing, 1997.

6. Nutritional Counseling: Anatomy and Physiology, American Health Science University, Independent publication, 1998.