



## Monograph

# Plant Sterols and Sterolins

## Introduction

Sterols and sterolins, also known as phytosterols, are fats present in all plants, including fruits and vegetables. Although they are chemically similar to the animal fat, cholesterol, they have been shown to exert significant unique biochemical effects in both animals and humans. Because they are bound to the fibers of the plant, they are difficult to absorb during the transit of digested food through the gut, particularly in individuals with impaired digestive function.<sup>1</sup> For this reason, and because much of the modern diet is over-processed and low in fresh plant materials, sterols and sterolins appear in the serum and tissue of healthy humans at 800-1000 times lower concentrations than that of cholesterol. Beta-sitosterol (BSS) is the major phytosterol in higher plants along with its glycoside, beta-sitosterolin (BSSG). Animal studies have demonstrated BSS and BSSG possess anti-inflammatory, antipyretic, antineoplastic, and immune-modulating properties. In other *in vitro*, animal, and human studies, a proprietary BSS:BSSG mixture has shown promise in normalizing T-cell function, dampening overactive antibody responses, and normalizing DHEA:cortisol ratios. Research has shown plant oils contain the highest concentration of phytosterols, nuts and seeds contain moderate amounts, and fruits and vegetables generally contain the lowest phytosterol concentrations.<sup>2</sup> Because only low levels of these substances are found in humans, increased dietary intake of unprocessed fruits and vegetables or supplementation with commercial phytosterols may be of benefit in re-establishing optimal immune parameters. Restoring balance to the immune system may be of therapeutic benefit in disease processes such as chronic viral infections, stress-induced immune suppression, tuberculosis, allergies, cancer, and rheumatoid arthritis and other autoimmune conditions.<sup>3,4</sup>

## Pharmacokinetics

Beta-sitosterol is not synthesized endogenously in man, and several animal studies over the last 70 years<sup>5-7</sup> have demonstrated its intestinal absorption in mammals is minimal, possibly as little as five percent of total dietary beta-sitosterol consumed. By comparison, intestinal absorption of cholesterol is 45-54 percent of intake. Unlike cholesterol, beta-sitosterol is rapidly secreted into the bile and is esterified outside the intestinal wall at a much slower rate.<sup>8</sup> Beta-sitosterol is secreted into the bile, stored in the gallbladder, and released intermittently into the duodenum, and subsequently incorporated into feces.

## **Mechanisms of Action**

### ***Anti-inflammatory/Antipyretic Agent***

Animal research of plant sterols given to rats demonstrated potent anti-inflammatory properties similar to cortisone. A proprietary blend of sterols and sterolins was capable of reducing the secretion of pro-inflammatory cytokines and tumor necrosis factor-alpha.<sup>1,9,10</sup> Phytosterols also reduced experimentally-induced edema. Animal research found antipyretic effects of phytosterols was comparable to that of aspirin.<sup>9</sup>

### ***Immune Modulation***

*In vitro*, animal, and human studies have shown that a 100:1 BSS:BSSG mixture is capable of enhancing several aspects of the immune response. By selectively enhancing activity of T-Helper-1 (T<sub>H</sub>1) cells and leaving unchanged or dampening the effect of T<sub>H</sub>2 cells, administration results in a significant rise in interleukin 2 (IL-2) and gamma interferon (IFN- $\gamma$ ) which enhance direct natural killer (NK) cell activity. Dampening of T<sub>H</sub>2 leads to decreased levels of interleukins (IL-4, IL-6, IL-10) involved in B-lymphocyte differentiation and inflammation. This combination also resulted in maintenance of cortisol and elevation of DHEA levels, thereby decreasing cortisol:DHEA ratios and buffering negative stress responses.<sup>10</sup>

### ***Blood Sugar Control***

The hypoglycemic properties of phytosterols were elucidated in an animal study using normo- and hyperglycemic rats. Results demonstrated that when either BSS or BSSG were given orally, fasting glucose levels were lowered and fasting insulin levels increased. This research also found beta-sitosterol was more effective over time in moderating glucose levels than its glycoside, beta-sitosterolin. It is thought phytosterol administration increases circulating insulin levels via stimulation of insulin secretion from pancreatic beta cells.<sup>11</sup>

## **Clinical Indications**

### ***Rheumatoid Arthritis***

Rheumatoid Arthritis (RA) is an inflammatory disease characterized by dysregulation of the immune system. B-lymphocytes become overactive and secrete antibodies that destroy synovial tissues of the joint. A BSS:BSSG combination was shown to increase the levels of T<sub>H</sub>1 cells, down-regulating antibody production by B-lymphocytes. The phytosterol mixture also decreased secretion of pro-inflammatory cytokines by macrophages, thereby decreasing inflammation. Most conventional RA treatments involve the use of drugs with significant side effects that are designed to control pain and suppress the entire immune response of the body, without addressing the actual immune dysfunction. By selectively activating or inhibiting certain aspects of the immune response, BSS:BSSG compounds can effectively regulate and control the overactive immune response seen in RA and other autoimmune diseases.<sup>1</sup>

### ***HIV/FIV Infection***

Animal and human research conducted in South Africa studied the effects of BSS:BSSG on disease progression of Feline Immunodeficiency Virus (FIV) and Human Immunodeficiency Virus (HIV). The initial positive studies were performed on cats infected with FIV (a feline retrovirus essentially equivalent to HIV) and prompted subsequent research on human subjects with HIV infection. Subjects given the sterol/sterolin mixture were able to maintain stable CD4 cell counts, and apoptosis

of CD4 lymphocytes declined slightly, thereby slowing disease progression. These studies also demonstrated a significant decrease in IL-6 levels, possibly slowing viral replication rates in infected cells and thereby decreasing viral load.<sup>12</sup>

### **Cancer**

A lack of secretion of IL-2 and IFN- $\gamma$  by T<sub>H</sub>1 cells leads to NK cells which are not capable of recognizing structures on the surface of tumor cells. Sterols and sterolins are known to increase secretion of IL-2 and IFN- $\gamma$ , enhancing NK cell activity and decreasing inflammation. A double-blind, placebo-controlled study of patients with cervical lesions caused by Human Papilloma Virus (HPV) is currently being conducted<sup>13</sup>

### **Benign Prostatic Hypertrophy (BPH)**

Two randomized, placebo-controlled, clinical studies were conducted on 350 men diagnosed with benign prostatic hypertrophy. Both studies lasted six months and dosages ranged from 60-130 mg beta-sitosterol daily. Although the exact mechanism is still unclear, beta-sitosterol administration resulted in improved peak urinary flow rate in both studies, as well as an improvement in subjective symptoms of BPH. Herbal remedies for BPH include saw palmetto, *Pygeum africanus*, and pumpkin seeds, and their effectiveness may be due to their phytosterol content. An herbal preparation for the treatment of BPH called Harzol, which contains beta-sitosterol and other phytosterols, has been available in Germany for the past 20 years.<sup>14,15</sup>

### **Immunosuppression in Endurance Athletes**

Marathon runners and endurance athletes often exhibit an increased inflammatory response to injury, as well as an immune suppression characterized by frequent bacterial and viral respiratory infections, all a result of high-intensity training. A double-blind study of marathon runners given a 100:1 BSS/BSSG mixture found improved maintenance of normal hematologic parameters, normalization of cortisol:DHEA ratios, and a decreased inflammatory response. This study indicates the phytosterol mixture acted to buffer cortisol release and its immunosuppressive effects.<sup>10</sup>

### **Diabetes**

Animal research found that in an oral glucose tolerance test BSS and BSSG protected test animals from an excessive rise in serum glucose levels due to glucose loading. This may be attributable to the fact that these phytosterols are capable of stimulating insulin secretion and thereby raising circulating insulin levels for better blood sugar control. The hypoglycemic effect of BSS and BSSG in animals indicates it might be an effective therapeutic tool for humans with diabetic and pre-diabetic conditions.<sup>11</sup> Also, due to their potential to down-regulate antibody production, this combination of sterols and sterolins may intervene in the inflammatory process associated with early-stage type 1 diabetes, protecting pancreatic beta cells from destruction.

### **Pulmonary Tuberculosis**

A double-blind, randomized, placebo-controlled trial was conducted with 47 culture-positive pulmonary tuberculosis patients. Patients were divided into two groups, hospitalized throughout the six-month long treatment, and treated with a standard regimen of isoniazid, rifampicin, and pyrazinamide. The test group also received a BSS:BSSG mixture. While several disease markers showed similar results between placebo and test groups, patients given the sterol/sterolin mixture showed a significantly faster weight recovery compared to the placebo group. Patients in the phytosterol group also exhibited

notable differences in certain hematological parameters, including increased lymphocyte, eosinophil, and monocyte counts. The results of this study suggest the immune modulating activity of phytosterols might be of therapeutic value in cases of multi-drug-resistant tuberculosis.<sup>16</sup>

## Ongoing Research

Ongoing research is being conducted with phytosterols and their effects on several other conditions, including chronic allergic rhinitis/sinusitis, asthma, and hepatitis C infection.<sup>17</sup>

## Dosage and Safety

Phytosterols are non-toxic, do not result in general immune suppression, and are rarely associated with side effects. Their high margin of safety make them an attractive therapeutic tool for a variety of conditions. The research has been conducted on a 100:1 BSS:BSSG formula containing 20 mg beta-sitosterol and 200 mcg beta-sitosterolin per capsule. A loading dose of two capsules three times daily should be given for one month, at which time this can be decreased to one capsule three times daily. Phytosterols work best if taken on an empty stomach, one hour before meals. They should not be taken with animal fats (including milk) as these foods inhibit absorption.

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