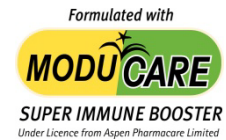


# Moducare Frequently Asked Questions

September 19, 2003



## What is Moducare®?

Moducare® is a patented blend of plant sterols and sterolins in a clinically proven ratio of 100:1. This formulation has been found to be effective at regulating the immune system -- enhancing an underactive immune system and/or modulating an overactive one. Plant sterols and sterolins are natural substances found in all fruits, vegetables, nuts and seeds. These plant nutrients have many unique health benefits. Unfortunately, we rarely get enough plant sterols and sterolins from our diets. The simplest way to get an optimal amount of these very beneficial natural compounds is by taking Moducare®.

## How should I take Moducare®?

*Adults:* One capsule 3 times daily OR two capsules upon arising and one capsule before bed. For best results, take with water or juice between meals on an empty stomach.

*Children:* One capsule per day for children under 5 years, two capsules per day for children between 5 and 12 years. Children over 12 years can take the adult dose.

For those with difficulty swallowing, the capsule can be opened and the contents mixed with applesauce or other fruit/vegetable.

## Why is the "sterolin" such an important part of the Moducare® formulation?

In nature, plants never contain sterols only. The sterols are always associated with their glucoside sterolin – a glucose molecule attached to the sterol molecule. The sterolin is easily destroyed through processing, freezing and some cooking methods. Without it, the sterol does not have the same immune-enhancing benefits.

## Is there any research behind this product?

Research on plant sterols has been underway since the 1920s. Dr. Patrick Bouic, Ph.D., at Stellenbosch University in South Africa, has been researching the exact combination of sterols and sterolins found in Moducare® for over a decade. There has been extensive testing and clinical trials, including double-blind, placebo-controlled studies. The work of Dr. Bouic and others has been published in international medical journals.

## Can I take Moducare® with my other supplements or medications?

There are no known interactions with Moducare® and any natural supplements. There is no conclusive evidence to suggest an interaction with medication. There has been an adverse event report in respect to a blood-thinning drug. An independent toxicology consulting firm assessed the report for our company and concluded that there is insufficient evidence to suggest that the adverse event arose from Moducare® use.

## Does Moducare® have any side effects?

When the immune system becomes balanced, some sensitive individuals may experience symptoms that indicate the body is trying to rid itself of toxins. These symptoms are temporary and may include digestive problems, rashes, headaches and fatigue.

### **Is Moducare® an immune "booster" like echinacea?**

The key difference between echinacea and Moducare® is that echinacea only stimulates the immune system, while Moducare® balances it. Echinacea is not recommended for prolonged use, or for people with autoimmune conditions. Moducare® allows the immune system to regulate itself: enhancing an underactive response and/or modulating an overactive one.

### **Do I take Moducare® for a few months and once my immune system is balanced, stop taking it?**

Moducare® is considered a daily supplement and should be taken as long as you want to aid the immune system to be balanced. Sterols and sterolins do not "fix" the immune system but provide the nutrients needed to help keep it in balance.

### **Is there anyone who should NOT take Moducare®?**

Recipients of foreign organs and tissues, including bone marrow and corneal transplants, are cautioned not to take any immune-regulating nutritional supplements. Therefore, Moducare® is NOT recommended for transplant patients. People with synthetic replacement/reconstruction will not be affected, e.g. hip, knee, breast, or pacemaker.

### **Are there any cautions associated with taking Moducare®?**

If you are pregnant, nursing, a diabetic, an organ transplant recipient or have multiple sclerosis, do not use unless on the advice of and under the direct supervision of a health care professional. To date, there have been two adverse event reports with respect to idiopathic thrombocytopenic purpura (ITP) and the use of sterol/sterolin-containing products. An independent toxicology consulting firm assessed these reports for our company and concluded that there is insufficient evidence to suggest that these adverse events arose from Moducare® use.

### **How long before I might expect to see some results?**

As with many natural supplements, it can take a period of time before you notice an improvement in your health. Although some people notice a difference sooner, we suggest that you take Moducare® for two to three months before evaluating whether it is effective for you.

### **MODUCARE® - A BRIEF HISTORY AND MODE OF ACTION**

Moducare® is a mixture of sitosterol\* (BSS) and its glucoside sitosterolin (BSSG) in a 100:1 ratio. This formulation was originally marketed in 1974 in Germany, after its beneficial effect in the treatment of benign prostate hypertrophy (BPH) had been established. Two years later, the same BSS/BSSG mixture was marketed in a product for rheumatoid arthritis.

In 1989, Professor Patrick Bouic and his colleagues at the Medical School of the University of Stellenbosch, Capetown, South Africa discovered that both sitosterol and sitosterolin have an immune modulating effect. Their findings, which were published in the *International Journal of Immunopharmacology* 1996, 18, 693-700, eventually resulted in the patented product called Moducare®.

Moducare® taken orally at 3 capsules per day (each capsule contains 20.2 mg sterols/sterolins) restores weakened or reduced T cell activity in a balanced proportion of T<sub>H1</sub> and T<sub>H2</sub> cells. This enables the immune system to effectively counteract viral diseases (common cold, hepatitis, HIV, etc.) and various microbial diseases (tuberculosis, etc.). Moducare® also corrects a variety of autoimmune conditions (e.g. rheumatoid arthritis) usually arising from an excess secretion of inflammatory factors. However, Moducare® is not a drug: it does not interfere with any metabolic processes of either the patient or an infecting agent but it is rather a catalyst or messenger initiating a correction of existing immune system imbalances or maintaining adequate existing balances. It thereby helps an individual to maintain good health or fight a disease effectively. The use of Moducare® is ideal in conjunction with drug treatments that tend to disturb the T<sub>H1</sub>:T<sub>H2</sub> balance or where a disease results in a T<sub>H1</sub>:T<sub>H2</sub> imbalance which a drug cannot correct.

\**sitosterol*: This compound is usually described in the literature as  $\beta$ -sitosterol or beta-sitosterol. The chemical name is often shortened to "sterol".

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### MONOGRAPH: MODUCARE®

Moducare® is a proprietary mix of plant sterols and sterolins in a clinically proven ratio of 100:1. This mixture is derived from a natural pine source and is encapsulated in a base of rice flour. The recommended dosage is one capsule three times per day to be taken between meals in the absence of any animal fats.

The Moducare® mixture has been shown to have immune modulating properties. It has been shown, both *in vitro* as well as *in vivo*, to have the following immunological activities:

- Enhances the cellular division of peripheral blood lymphocytes when these are activated by stimuli [1];
- Enhances the killing ability/cytotoxicity of specialized cells responsible for immune surveillance, namely the Natural Killer cells (NK cells) [1];
- Enhances the ability of T lymphocytes to release the factors that ultimately regulate cellular functions in the body. These T cells ( $T_{H1}$  helper cells) are antagonist to the activity of other helper cells ( $T_{H2}$ ) that promote the functions of B lymphocytes [2];
- The mixture of sterols/sterolins has anti-inflammatory properties by switching off the release of pro-inflammatory factors such as Interleukin 6 (IL6) and Tumor Necrosis Factor-alpha (TNF- $\alpha$ ) from activated monocytes [3];
- Increases the secretion of IL12, the cytokine released from antigen-presenting cells that promotes the differentiation of precursor T-helper cells into the more polarized  $T_{H1}$  cells;
- The mixture has adreno-cortical effects by decreasing the cortisol:DHEA ratio suggestive that it enhances the synthesis of DHEA which ultimately, decreases the release of cortisol [4].
- Numerous clinical studies have shown the efficacy of plant sterols/sterolins *in vivo*. Based on the biological activities described above, most studies to date have investigated the ability of Moducare® to control inflammation or induce a shift from a predominantly humoral immune response to a more protective cellular response (i.e.  $T_{H2}$  to  $T_{H1}$  shift). Therefore, studies have been conducted in several infectious diseases as well as chronic inflammatory conditions and in models of immune stress. Briefly, these include:
- The investigation of Moducare® as adjuvants in the treatment of pulmonary tuberculosis. This double-blind, placebo-controlled study showed that patients having received the capsules containing the sterols/sterolins had less inflammation, recovered from the mycobacterial infection faster (faster resolution of lung lesions) and recovered their immunological status faster [5]. Other markers of efficacy included higher weight gain. All patients had received standard anti-tuberculosis therapy.
- The sterols/sterolins mixture was tested in a clinical study (double-blind, placebo-controlled) conducted in marathon runners, a model of the effects of excessive exercise on the immune system. Such individuals are prone to transient immune suppression due to the activation of several endocrinological shifts that ultimately lead to decreased immunity. This study showed that the marathon runners had less inflammation post event (lower IL6 plasma levels), less haematological disturbances (less lymphopaenia and less neutrophilia in the peripheral blood) and maintained their adreno-cortical status compared to their baseline values [6]. The study thus showed that Moducare® was able to abrogate the immunological shifts that usually accompany endurance exercise.
- The use of the mixture by HIV-infected individuals has been extensively studied [7]. It has been shown to prevent the decline of CD4 cell numbers (a surrogate marker of disease progression), decrease the plasma viral loads of patients and maintain a relatively intact immune profile despite the chronic viral infection. This implies that the use of the immune modulator by HIV-infected individuals would prevent the deterioration of the immunity and the maintenance of effective cellular responses to the virus [8].

- In a clinical model of chronic inflammation, Rheumatoid arthritis patients were followed over a period of 6 months and this study (double-blind, placebo-controlled) showed attenuation of indices of disease activity due to the potent anti-inflammatory properties of the sterols/sterolins [9].
- In an open-labeled study, allergic rhinitis and sinusitis patients were followed over a period of 12 weeks and again, the degree of allergic responses showed significant changes accompanied by clinical improvement and symptomatic relief of patients. Markers of efficacy included decrease in serum IgE levels, decrease in the T<sub>H2</sub> cell activity, less turbinate hypertrophy and rhinorea, etc [10].

To date, no drug-drug interactions have been observed in patients using Moducare®. It is advisable for patients to inform their clinicians of their intention to use this supplement. It has to be understood that it does not replace conventional medication, especially those used for life-threatening diseases. Moducare® should be viewed as an adjunct to help shift the immune responses to a more balanced status and to control chronic inflammation.

At present, patients having received solid organ or tissue transplants should avoid the use of this immune modulator. This is based on the ability of the sterols/sterolins in the current formulation to promote cellular immune mechanisms, the same mechanisms being responsible for graft rejection.

Patrick J.D. Bouic, Ph.D., August 2002

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Moducare® is manufactured by EPI (Essential Phytosterolins Inc).

For information call 877-297-7332 or visit our website at [www.moducare.com](http://www.moducare.com)