

Sterols/Sterolins, Natural, Nontoxic Immunomodulators and Their Role in the Control of Rheumatoid Arthritis

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Introduction

Autoimmune diseases, including rheumatoid arthritis (RA), are the result of malfunction of the immune system, activated by an unknown agent to attack and destroy the host's tissues. Many reasons for dysfunction of the immune system have been postulated by medical researchers, but the standard approach to the treatment of such patients has been to suppress the immune response with immunosuppressive drugs, regardless of their many damaging side effects. Other treatments offered are merely palliative, designed to relieve pain and other symptoms linked to the inflammatory process.

Recent research conducted on sterols and sterolins (plant fats) by our group at Tygerberg Hospital/University of Stellenbosch Medical Faculty and published in the *International Journal of Immunopharmacology*, is providing an entirely new medical approach to the treatment of auto-immune and other chronic diseases which only manifest themselves when the immune system of afflicted individuals is compromised.

The following is a summary of how the immune system functions under a normal response and how during a pathological process, the same system can cause the tissue damage seen in various diseases. A normal healthy immune system relies on:

- B cells which produce antibodies (proteins) which destroy invading pathogens such as bacteria, viruses, parasites and other foreign proteins before they can enter the cells of the host.
- T cells which are the cells controlling and regulating the immune response. These are divided into either CD4 positive (also called the T-helper cell) or CD8 positive (called the T suppressor or cytotoxic cell).

To complicate the matter, there are 2 types of T helper cells: the so-called TH1 CD4 cells which produce IL2 (interleukin 2) and Gamma Interferon (IFN-g) and, the TH2 CD4 cells which release IL4, IL6 and IL10 which enhance the activity of B cells to produce antibodies.

Should the activity of TH1 CD4 cells be defective, many chronic diseases typified by an over-activity of antibody production ensue. On the other hand, the CD8 positive cells are activated by the TH1 lymphokines to become killer/cytotoxic cells which kill the host cells which harbor the pathogen: this is an escape mechanism utilized by certain organisms in an attempt to evade the initial response mounted by the antibodies produced by the B cells. This is due to the fact that, once inside the host cell, the pathogens are inaccessible to the action of antibodies. Hence, the cellular mechanism typified by the CD8 T cells evolved as a result of this escape mechanism employed by the pathogens in question.

The immune system is finely tuned to adapt to changes which can be induced either when a virus or bacterium invades the host or to recognize changes that are associated with the development of malignant characteristics. It therefore stands to reason that when the TH1 arm of the T cells is deficient, the consequence is one of infection, chronic inflammation and eventually tissue damage and disease.

Plant Sterols/Sterolins: What Are They and How Do They Modulate the Immune Response?

Plant sterols and sterolins are amongst the many phytochemicals (biologically active molecules isolated from plants) which have, in recent years, stimulated research into the healing and

protective effects of plants. Both sterols and sterolins were identified and chemically elucidated as early as 1922. They are plant "fats" present in every single plant (fruits and vegetables) and although chemically very similar to the animal fat, cholesterol, they are totally different in biological functions. In the natural state, they are bound to the fibers of the plant and for this reason, they are difficult to desorb from the fibers during the normal transit of digested food through our gut, especially in the case of older people whose digestion is less effective than that of a younger person's. Seeds are the richest source of the sterols and sterolins and yet, the refining processes applied in the food industry render the staple foods useless because they remove the sterols and sterolins to make the product more appealing to the eye (for instance, in order to prevent the precipitation of the fats in so-called cold pressed oils, the oil is heated and refined to remove the sterols/sterolins). Also of importance is the fact that our modern diet is low in fresh plant materials (vegetables and fruits) because we have recourse to the fast food outlets or we are generally carnivorous and do not consume sufficient fruits and vegetables.

Sterols and sterolins have been shown to modulate the functions of the T cells both *in vitro* and *in vivo* by enhancing their cellular division and their secretion of these important regulatory soluble factors called lymphokines (IL2 and IFN- γ). It is important to note that only the function of the so-called TH1 cells seem to be enhanced, leaving the activity of the TH2 helper cells unaffected. This is crucial because it is these specific lymphokines which are responsible for controlling the activity of the B cells.

Sterols/Sterolins

Both IL2 and IFN- γ are able to switch off the release of the lymphokines which help the B cells to make antibodies.

In the case of rheumatoid arthritis, it is thought that the over-activity of the B cells is directly involved in the release of antibodies which attach themselves to the synovial tissue and the destruction thereof. Also, the antibodies form complexes with other antibodies and precipitate within a joint: this is thought to initiate the entire process of inflammation.

It has been shown that the secretion of inflammatory cytokines released by macrophages is very effectively inhibited by the sterols/sterolins. We have shown that the synthesis and release of both IL6 and TNF- α (both factors are referred to as pro-inflammatory factors because they initiate and maintain inflammation) are switched off when macrophages are cultured in the presence of a mixture of sterols/sterolins. This work confirms earlier observations in an animal model (rats) in which an inflammatory process was inhibited by pretreatment with sterols/sterolins. It appears the plant fats offer effective anti-inflammatory activity at sites of chronic inflammation by switching off the very factors which initiate the process.

Evidence for Involvement of the Immune Response and Its Mediators in the Disease Process of Rheumatoid Arthritis

Synovium from a patient afflicted with RA contains the cellular infiltrate made up of T cells, macrophages and B cells. At sites of active tissue destruction, very high levels of cytokines (eg. IL1, IL6, and TNF- α) are directly involved in the inflammatory process and this destruction can be prevented by specific cytokine inhibitors. Furthermore, it has also been shown that damage can be induced in normal healthy cartilage by adding the fluid from a rheumatoid arthritis patient's synovium to the healthy cartilage.

More recently high levels of TH2 cells (as opposed to TH1 cells) have been discovered in the synovium of RA patients. It appears that TH2 cytokines may be directly involved in the destruction of the synovium by antibodies which we often refer to as rheumatoid factors (RFs). RFs form complexes with other antibodies and often precipitate at the site, initiating recruitment of inflammatory cells. These immune complexes can be demonstrated in the synovial fluid and even the serum of RA patients.

Understanding the modulatory activity of sterols/sterolins, it is not surprising that these plant fats are beneficial in control of this chronic disease. We have been able to show that sterols/sterolins enhance preferentially, the activity of TH1 cells and inhibit the synthesis and release of other inflammatory factors. The disease can therefore be controlled by reversing the immune abnormality at the site of disease, preventing damage caused by inflammation.

The major differences between the use of conventional medicines and the sterols/sterolins in the control of rheumatoid arthritis is that conventional drugs are mainly aimed at inhibiting the entire immune response and the inflammatory process with the use of anti-inflammatory compounds and immunosuppressive drugs (cortisone, etc). Such treatments are not without side effects and dangers because of their non-specificity. Chronic use of immunosuppressive medications eventually leaves the individual totally open to infections. Such immune-suppressed patients are also more prone to development of cancer.

Sterols/sterolins are entirely different in their function in that they target the abnormality, correcting the immune dysfunction. Many factors can lead to malfunction of the immune response, including infection by pathogens which specifically target TH1 cells (eg. HIV), chronic stress (physical

as well as psychological), and poor nutrition. It therefore stands to reason that many chronic diseases could be totally preventable by ensuring the intake of essential micronutrients, including sterols and sterolins.

The major advantage of the use of sterols/sterolins in the management of rheumatoid arthritis is that these fatty plant constituents are natural, non-toxic, and without side effects (no general immune suppression). This revolutionary approach to the treatment of autoimmune diseases will certainly be the approach of the future.

Note: According to Dr. Bouic, "The company that has sponsored the above reported research has encapsulated these molecules and the recommended dosage is 1 capsule 3 times per day on an empty stomach. There is no drug-induced adverse effects based on the usage of the capsules by over 25,000 clinical trial volunteers. The company is currently marketing the capsules here in South Africa under the trade name of ModuCare™. It is available retail in Canada from Purity Life and in the US from Natural Balance and Rexall Sundown. The sole provider for licensed health care professionals is Thorne Research. The formulation is patented internationally including the United States, and any questions should be directed to the sponsoring company in South Africa at telephone number 27-11-3151430 or fax 27-11-3151462.

Dr. Bouic is currently running a placebo-controlled double blind trial in rheumatoid arthritis patients using ModuCare™, eventually to be published in a peer-reviewed journal. Most of the data to date has been based on individual cases.