STEROLS/STEROLINS, THE NATURAL, NONTOXIC IMMUNO-MODULATORS AND THEIR ROLE IN THE CONTROL OF RHEUMATOID ARTHRITIS

Prof. Patrick JD Bouic, Chief Specialist Scientist, Head: Immunology, Department of Medical Microbiology, Tygerberg Hospital/University of Stellenbosch, Faculty of Medicine, PO Box 19063, 7505 Tygerberg, South Africa.

INTRODUCTION:
It is a well known fact that all auto-immune diseases, of which Rheumatoid arthritis (RA) forms a large portion, are the result of the malfunction of the body’s immune system which is activated by an unknown agent to attack and destroy the host’s tissues. Many reasons for the 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, notwithstanding their many damaging side effects. Other treatments offered are merely palliative and designed to relieve pain and symptoms linked to the inflammatory process.

Recent research conducted on the 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 diseases and other chronic diseases which only manifest themselves when the immune system of afflicted individuals is at cause. International medical and scientific interest in this breakthrough has been overwhelming and a number of clinical trials using sterols and sterolins for various conditions are far progressed and more are planned in the near future.

With the millions of people suffering from RA and other auto-immune diseases in mind, any new information coming to light will be published at the earliest opportunity.

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:** these produce antibodies (proteins) which destroy invading pathogens such as bacteria, viruses, parasites and other foreign proteins before they have entered the cells of the host.
- **T cells** are the cells which control and regulate the immune response. These are divided into:
  - either CD4 positive (or also called the T-helper cell) or,
  - CD8 positive (or called the T suppressor or cytotoxic cell).

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

In fact, it is known that 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 in that they 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 pathogen 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. (See “Immune System Protection from Foreign Invaders,” http:www.arthritistrust.org.)

**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 factors called lymphokines (IL2 and gIFN). 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. Both IL2 and IFN-g are able to switch off the release of the lymphokines which help the B cells to make antibodies.

Now 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.

Furthermore, 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-a (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 made by using an animal model (rats) in which an inflammatory state was induced in the paws of the animals using artificial agents. However, the pre-treatment of the animals with sterols/sterolins resulted in the absence of such inflammation.

The above therefore indicates to us that the plant fats are capable of carrying out a natural anti-inflammatory activity at sites where the chronic inflammation is present. This they do by switching off the very factors which initiate the process.

**EVIDENCE FOR THE 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, it has been shown that there are very high levels of the cytokines directly involved in the inflammatory process (eg. IL6, TNF-a and IL-1) and this destruction can be prevented by specific inhibitors or molecules which counteract the activity of these factors. 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, it has been shown that when one looks into the types of T cells infiltrating the synovium, such cells are pre-dominantly of the TH2 type rather than of the TH1 type. To re-activate the T cells infiltrating the synovium, such cells are vented by specific inhibitors or molecules which counteract the high levels of the cytokines directly involved in the inflammatory process. We have shown that when one looks into the types of T cells infiltrating the synovium, such cells are pre-dominantly of the TH2 type rather than of the TH1 type. To re-activate the T cells infiltrating the synovium, such cells are vented by specific inhibitors or molecules which counteract the high levels of the cytokines directly involved in the inflammatory process. We have shown that when one looks into the types of T cells infiltrating the synovium, such cells are pre-dominantly of the TH2 type rather than of the TH1 type. To re-activate the T cells infiltrating the synovium, such cells are vented by specific inhibitors or molecules which counteract the high levels of the cytokines directly involved in the inflammatory process. We have shown that when one looks into the types of T cells infiltrating the synovium, such cells are pre-dominantly of the TH2 type rather than of the TH1 type. To re-activate the T cells infiltrating the synovium, such cells are vented by specific inhibitors or molecules which counteract the high levels of the cytokines directly involved in the inflammatory process. We have shown that when one looks into the types of T cells infiltrating the synovium, such cells are pre-dominantly of the TH2 type rather than of the TH1 type. To re-activate the T cells infiltrating the synovium, such cells are vented by specific inhibitors or molecules which counteract the high levels of the cytokines directly involved in the inflammatory process.

The sterols/sterolins are entirely different in their function in that they are targeted at the abnormality and they correct these immune dysfunctions. Many factors can lead to the malfunction of the immune response, especially that represented by the regulatory T_{H} subset of CD4 cells. These may include infection by specific pathogens which target these specific cells (for example the HIV) but other factors such as chronic stress (physical as well as psychological) and bad nutrition can ultimately lead to the same end result. It therefore stands to reason that many chronic diseases are totally preventable by ensuring the intake of the essential micro-nutrients, sterols and sterolins. They are also anti-inflammatory in activity in that they are able to switch off the factors which maintain the inflammatory process.

The major advantage of the use of sterols/sterolins in the management of rheumatoid arthritis is that the plant fats 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 f the capsules by over 25,000 clinical trial volunteers. The company is currently (2001) marketing the capsules in South Africa under the tradename of ModuCare and hopefully this will shortly be available in North America. The formulation is patented internationally including the United States and should any requests for the product arise as a result of this article, these should be directed to the sponsoring company at South Africa telephone number 27-11-3151430 or Fax 27-11-3151462.

Dr. Bouic is currently (2001) finalizing the protocol for a placebo-controlled double blind trial in rheumatoid arthritis patients using the ModuCare and as soon as the results of this trial are available, they will be forward to The Arthritis Trust of America, 7111 Sweetgum Drive SW, Suite A, Fairview, TN 37062-9384. “Most of the data to date has been based on individual cases.”

Also, a North American Source for sterols/sterolins is Essens Phytoesterolins, Inc., 6 Commerce Crescent, Acton, Ontario, Canada L7J 2X3; (519) 853-1129; Fax (519) 853-4660

**Summary**

**STEROLS AND STEROLINS - WHAT ARE THEY?**

- One of the many phytochemicals 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). Chemically very similar to animal fat, cholesterol, but totally different in biological functions.
- Sterols never exist on their own: always in combination with their glucosides.
- In the natural state, they are bound to the fibres of the plant and for this reason, they are difficult to desorb from the fibres.
- Seeds are the richest source of the sterols and sterolins; and yet, the refining processes applied in the food industry render the foods useless because they remove the sterols and sterolins to make the product more appealing to the eye (such as no precipitation of the fats in the extracted oils from seeds).
- Also of importance is the fact that our diet is low in plant materials (vegetables and fruits) or we have recourse to the fast food outlets!!
- The way in which we prepare our vegetables is also a major cause for concern: we freeze the vegetables (which releases en-
The immune system and its dependence on sterols and sterolins:

- Our immune system is made up of several cells and the factors which they secrete in response to an invading offender.
- On one hand we have cells called B lymphocytes which make proteins (antibodies) which bind to and inactivate the organism only if the organism is on the outside of the host’s cells (for example, a bacterium). Once the organism has been internalized, it is inaccessible to the action of the antibodies. This was a ploy developed by microorganisms in order to evade the immune system.
- On the other hand, the T cells are specialised cells which fight off offenders which live inside the host’s cells (eg. viruses, certain bacteria, etc). The T cells secrete soluble factors which enhance the functions of specialised cytotoxic cells which kill off the infected cells.
- Sterols and sterolins have been shown to modulate the functions of the T cells by enhancing their cellular division and their secretion of these important soluble factors called lymphokines. Also, the activity of the cytotoxic cells is greatly promoted in the presence of the sterols/sterolins mixture. These activities are of utmost importance in fighting off viral diseases or diseases involving bacteria which live inside cells (eg tuberculosis).
- It should be noted that the enhancing activity described above is maximal when both the sterols and sterolins are present. It was previously shown that the absorption of the sterols is increased when in conjunction with the sterolins and vice versa. It therefore stands to reason that both are required to carry out this immunological activity.
- Hence, under ideal and healthy conditions whereby the person is taking the sterols/sterolins mixture, the cells of the immune system are “primed” to function optimally so that an infection is taken care of quicker and more efficiently.
- In certain diseases, the immune system starts to attack one’s own body by producing antibodies directed to the host’s body constituents. These are called autoimmune diseases (eg. Rheumatoid arthritis, Systemic Lupus Erythematosus or SLE, Multiple Sclerosis, etc) and these are known to arise in response to an overproduction of lymphokines which promote the functions of B cells making the antibodies. If the “correct” lymphokines could be secreted by the T cells then one should be able to correct the disease process and the disease would be alleviated. In other words, the sterols/sterolins mixture treat the underlying causes and not the symptoms.
- Other diseases/conditions which would benefit from the intake of sterols/sterolins mixture include:
  1. Cancer: it is known that the individual’s immune system is low thereby allowing the growth of cancer cells. By enhancing the function of both T cells and the secretion of lymphokines, it can be predicted that the cancer cells will be attacked and killed.
  2. Allergies: in these conditions, the lymphokines secreted by the T cells promote the B cells to make a certain type of antibodies (IgE). Because the sterols/sterolins mixture stimulate the secretion of “good” lymphokines which inhibit the IgE promoting lymphokines, the symptoms of an allergic state would disappear.
  3. Chronic viral diseases: such as HIV infection where it is known that the immune suppression is due to the body’s immune system failing to make sufficient lymphokines which stimulate the activity of cytotoxic T cells (hence chronic infection) and also the T cells fail to divide in response to the invading virus or other opportunistic organisms. Since the sterols/sterolins stimulate both the proliferation of lymphocytes when these have to respond to organisms as well as the secretion of lymphokines, in these diseases, the individuals would find that their immune system would cope with the onslaught by the invading organism and that there would not be destruction of the immune cells which normally accompanies infection by HIV.

(c) Chronic viral diseases: such as HIV infection

(d) Stress: the killer of modern man. It is a well known fact that stress (either physical or mental) has a detrimental effect on the immune system due to the synthesis and release of hormones such as Cortisol. It has been the interest of prominent immunologists and sports medicine doctors to find out why marathon runners are prone to colds and influenza during the period immediately following a marathon run. It is now known that during the excessive physical stress, the immune system is inhibited by the secretion of cortisol and the increased release of proinflammatory factors (due to tissue damage). Sterols/sterolins have been shown to reverse these process and to prevent the post-marathon infections: indeed, the plant sterols/sterolins decrease the blood levels of cortisol as well as the factors which themselves induce inflammation (tissue damage, muscular aches and stiffness, etc.). (See “Stress,” http://www.arthritistrust.org.)