The Arthritis Trust

Dedicated to Eradicating Rheumatoid Disease From the Earth

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STEROLS/STEROLINS:

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

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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 systems 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 T_{H1}CD4 cells which produce IL2 (Interleukin 2) and Gamma Interferon (IFN-g) and the T_{H2}CD4 cells release IL4, IL6 and IL10 which enhance the activity of B cells to produce antibodies. In fact, it is known that should activity of T_{H1}CD4 cells be defective, many chronic diseased typified by an over-activity of antibody production ensue.

On the other hand, the CD8 positive cells are activated by the T_{H1} lymphokines to become killer/cytotoxic cells in that they kill 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 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 theT_{H1} arm of the Tcells

(continued on page 4)

Sterols/Sterolins

(continued from page 1)

is deficient, the consequence in 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 plant) 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 at 1922. They are plant "fats" present in every single plant (fruit 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 fibres of the plant and for this reason, they are difficult to desorb from the fibres 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 in both *in vitro* and *in vivo* by enhancing their cellular division and their secretion of these important regulatory soluble factors called lymphokines (IL2 and g-IFN). It is important to note that only the function of the so-called T_{H1} cells seem to be enhanced leaving the activity of the T_{H2} 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-α (both factors are referred to a 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 indicated 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 inflammation process (eg. IL6, TNF-a and IL-1) and this destruction can be prevented by specific inhibitors or molecules which counteract the activities 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 T_{H2} type rather than of the T_{H1} type. To recall, the T_{H2} helper cells secrete the growth factors which help the B cells to change into antibody factories and to make more of these proteins. Hence, it stands to reason that the T_{H2} cytokines are directly involved in the destruction of the synovium by the antibodies which we often refer to as the rheumatoid factors (RF's). These RF's form the complexes with other antibodies and often precipitate at the site and thus initiate the recruitment of the inflammatory cells. These complexes (also called immune complexes) can be demonstrated in the synovium fluid and even the serum of patients.

When one recalls the modulatory activity of the sterols/sterolins, it is not surprising that these plant fats are beneficial in the control of this chronic disease. Indeed, we have been able to show that the sterols / sterolins enhance preferentially the activity of T_{H1} cells and also inhibit the synthesis and release of other factors which induce inflammation. We are therefore able to control the disease by preventing the damage caused by the inflammation but more importantly, we are able to reverse the immune abnormality at the site of the disease.

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, hence the use of anti-inflammatory compounds and immunosupressives (cortisone, etc). Needless to say, such treatments are not without side effects and dangers because of their non-specifity and we all know that chronic use of immunosupressives eventually leaves the individual totally open to opportunistic infections (or even common infections) because the immune system is kept suppressed to protect the body from the onslaught by the immune response. More seriously, it should also be remembered that such immune suppressed patients are more prone to the development of more life threatening tumors and carcinomas.

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_{H1} CD4 cells. These may include infection by specific pathogens which target these specific cells (for example 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 stand 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 to 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 revolution-

(continued on page 7)

Sterols/Sterolins

(continued from page 4)

ary 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 are 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 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 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 forwarded to The Arthritis Trust of America, 7111 Sweetgum Drive, S.W., Suite A, Fairview, TN 37062-9384. "Most of the data to date has been based on individual cases."

Arthritis/Rheumatism

Letters To Your Editor