Clinical Efficacy of Systemic Enzyme Support  
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Clinical observations and literature review both affirm the conviction that systemic enzyme support with Wobenzym® N or Wobenzym® PS is an essential component for successful management of inflammation disorders and other conditions with immune system dysregulation due to its high degree of clinical efficacy. In addition to improving clinical outcomes in conditions with overt inflammation, such as rheumatoid arthritis, thrombophlebitis, pyelonephritis, prostatitis and psoriasis, systemic enzyme support is also affective in conditions with covert inflammation such as osteoarthritis, angina, atherosclerosis, myocardial infarctions, and diabetes to name a few. The adjuvant properties of systemic enzyme support have also been observed and documented for a number of cases including adnexitis, arthritis, papillomas and various forms of cancer. This article will familiarize clinicians with the therapeutic benefits of systemic enzyme support and review pertinent findings related to this treatment modality.

Enzymes are biological molecules that increase the rate of chemical reactions. In the human body, thousands of chemical reactions occur during the course of normal metabolic processes. These reactions require significant energy in order to take place. Enzymes act as catalyst to lower the energy needed for the reaction to move forward. As such, enzymes maintain optimal function of the various systems in the body and support overall good health and optimal quality of life.

The immune system is very dependent on proper enzyme function in regards to regulating inflammation as well as protecting cells from damage. Cytokine activity, and the clearance of excessive inflammatory cytokines, is regulated by proteases, enzymes which degrade proteins. The clearance of tissue proteins and peptides damaged by inflammation is also mediated by proteases. Proteases significantly reduce concentrations of advance glycation end-products (AGEs) and protect cells by decreasing their receptor (RAGEs) activation. Proteases also down-regulate adhesion molecule activity in inflamed, as well as malignant cells.

Inflammation Observed
This inflammation response can be quite aggressive, and manifest as the five cardinal signs of inflammation recognized ages ago: redness, heat, swelling, pain and loss of function, classically referred to in Latin as *rubor, calor, tumor, dolor & functio laesa*. Pain, loss of function, and other cardinal signs of inflammation diminish our quality of life and may be a harbinger of serious disease. Therefore, clinically evident inflammation is often recognized as the body communicating an inability to control proper cellular processes.

In addition to the clinical signs of inflammation, laboratory tests often show increased levels in the various biomarkers of inflammation that are also associated with increased morbidity and mortality. These include the well known erythrocyte sedimentation rate (ESR) and C-Reactive Protein (CRP). Circulating
Immune Complexes (CICs), and immunoglobulins (IgG, IgE, IgA & IgM) are often elevated by excessive inflammation. Excessive fibrin activity and increased amyloid beta-peptide can also be quantified in the presence of imbalanced inflammation. Certain cytokine levels may also increase, which may cause further imbalance in the immune system. The change in certain cytokine levels is of specific interest because it allows us to recognize when the immune system has become significantly imbalanced, and provides us with insight into how immunomodulation can be achieved through the use of systemic enzymes.

**Inflammation & Cytokines**

Cytokines are signaling proteins and glycoproteins involved in cellular communications that play a dominant role in maintaining the normal inflammatory processes of the immune system. Cytokines such as interferon-gamma (INF-γ), tumor necrosis factor-alpha (TNF-α), transforming growth factor beta (TGF-β) and interleukins (IL-2, IL-6, IL-12, IL-4, IL-5, IL-10) are produced de novo (on demand) in various cells as a direct response to stimulation of the immune system. They are produced by a wide variety of cells and are typically subdivided into two categories, Th1 & Th2. A balance between Th1 and Th2 responses is best for optimal health.

Th1 cytokines tend to produce the pro-inflammatory responses involved in antibacterial, antiviral and antifungal responses. Excessive Th1 responses can lead to uncontrolled tissue damage and may perpetuate autoimmune responses. A relative excess in Th1 is also observed in acute inflammation. Th2 cytokines tend to produce anti-inflammatory responses and can counteract the Th1 mediated microbicidal actions. Excessive TH2 responses are associated with allergies and atopy (asthma, eczema, allergic rhinitis & allergic conjunctivitis). A relative excess in Th2 is also observed in chronic inflammation.

The binding and removal of excessive cytokines is mediated by α-2-macroglobulin (alpha 2-macroglobulin), a naturally occurring high molecular weight plasma glycoprotein. Proteases bind with α-2-macroglobulins to create α-2-macroglobulin-protease complexes and transform the α-2-macroglobulin from its native form into the active form. Systemic enzyme support increases endogenous proteases and supports the activation of α-2-macroglobulin. The newly activated α-2-macroglobulin-protease complex now has increased binding capacity for certain cytokines, as well as other proteins and glycoproteins. Protease activation of α-2-macroglobulin also facilitates its binding to, and elimination of, proteins damaged by oxidative stress or heat as well as the degradation and clearance of the amyloid beta peptide (A beta), a major component of senile plaques in Alzheimer’s patients. These activated alpha 2-macroglobulin-proteinase complexes, which now bind excessive cytokines and damaged proteins, are also activated for receptor mediated endocytosis when they were transformed by the protease enzymes. Therefore, these complexes, as well as the cytokines and debris they carry, are quickly removed by hepatic α-2M-receptors (α-2M-R), and other cells expressing α-2M-R, such as macrophages. The removal of damaged proteins, cellular debris, and unwanted peptides (such as amyloid beta peptides) are normal immune system responses to defend the body from all pathogenic influences – whatever their origin – whatever their size.
Since excessive cytokines are involved in auto-aggressive inflammatory processes, the binding to cytokines and the removal of cytokines by the activated α-2-macroglobulin proteins support a balanced and properly functioning immune system. Therefore the removal of excessive cytokines allows the immune system to restore Th1/Th2 balance. Once cytokine levels are restored to their optimal physiologically balanced state the immune system is able to resume its function of protecting the body and initiating the healing process. With renewal of the normal inflammatory process the regenerative processes of the immune system are again allowed to function.

**Restoring Immunostasis**

As noted, the clearance of excessive cytokines, the clearance of proteins and peptides damaged by inflammation, the inactivation of advance glycation end-products, and the inactivation of adhesion molecules in inflamed and malignant cells are all mediated by proteolytic enzymes. A balanced immune system – immunostasis – can be manifested by using systemic enzyme support, which provides the essential proteolytic enzymes. Systemic enzyme support can be defined as a treatment modality which uses oral administration of exogenous hydrolytic (mainly proteolytic) enzymes of animal origin (trypsin, chymotrypsin) and plant origin (bromelain, papain) in the form of enteric-coated tablets for supporting healthy and normal inflammatory processes in the body.

Systemic enzyme support (SES) which uses Wobenzym® N and Wobenzym® PS - clinically validated formulations of enzymes from both plants and animals - is able to influence immunity in such a fashion as to reduce pain, swelling, inflammation, edema and lymphedema, and increase fibrinolysis, and the clearance of harmful immune complexes that are a result of antibody reactions. SES provides enzymes which can be utilized to assist the body’s various regulatory and communications systems and supports the function of tissues at a cellular level. SES has application for degenerative diseases, autoimmune diseases, and as an adjuvant to improve efficacy of anti-infectives in infectious diseases.

A significant amount of the published international literature describing the clinical benefits of systemic enzyme support is based on various systemic enzyme support formulations made for many decades by MUCOS Pharma, a Germany pharmaceutical company. Even after the sale of MUCOS Pharma, Wobenzym® N is still manufactured in Germany, but is distributed by MUCOS, LLC, an American company.

The history of Wobenzym® is significant in that systemic enzyme support requires sophisticated processing techniques to be effective. Systemic enzyme support formulations are considered prescription drugs in part of Europe, and manufactured to the same high standards of pharmaceuticals. The Wobenzym® N and Wobenzym® PS enteric coated, animal enzyme, plant enzyme and rutosid combinations are the most researched systemic enzyme formulations in the world; and used by athletes, doctors and millions of people to help normalize inflammation, speed recovery from sports and other routine injuries, and promote healthy circulation.

The active constituents in Wobenzym® N and Wobenzym® PS are delivered through tablets that have a special enteric coating which can withstand the acid environment in the stomach, which is important since enzymes can be damaged by stomach acid. Once the tablet has passed a safe distance from the
stomach acids, the tablet dissolves and the enzymes are efficiently absorbed by the mucosal membrane of the intestine. This process is most effective if the tablets are taken away from meals.

**Conditions Treated with Systemic Enzyme Support**

Based on clinical observations and literature review systemic enzyme support effectively improves the treatment of conditions with an auto-aggressive component by promoting the decomposition and elimination of disease associated circulating immune complexes. Improvements in CRP, ESR and other biomarkers of inflammation are also noted. Clinical improvement is noted in a wide range of conditions, with benefits observed in treating various body systems. Nervous system disorders such as multiple sclerosis showed a decreased number and duration of attacks because of decreased inflammatory activity due to systemic enzyme support. A notable increase in the degradation and clearance of the amyloid beta (A beta) peptide can reduce the risk of developing Alzheimer's disease.

The cardiovascular system benefits by reduced risks of re-infarction after an MI because of the hypolipidemic and immunonormalizing benefits of systemic enzyme support. Patients with stable angina pectoris had a demonstrable reduction in the frequency and intensity of angina pectoris attacks and increased tolerance of physical work load with systemic enzyme support. Disease of venous system, including acute thrombophlebitis and postthrombophlebitic syndrome were dramatically improved by systemic enzyme support, with a notable decrease of pain, reduction of edema and trophic ulcers. Other research showed highly effective resolution of lymphedema in both upper and lower extremities due to fibrinolytic & antiedematous effects of systemic enzyme support.

Respiratory system health is improved by systemic enzyme support with a notable reduction of both frequency and severity of recurrent respiratory tract infections. Researchers have concluded that systemic enzyme support represents a novel therapeutic modality helping in the treatment of children showing a high sickness rate and note that the as number and severity of dyspnea attacks decreased in children with proven asthma.

Integumentary conditions had improved clinical success when systemic enzyme support was added as an adjuvant with other conventional therapies. The inclusion of systemic enzyme support in treatment of psoriasis significantly decreases the exudative component of exacerbation, increased regression and decreases recurrence. Eczema (atopic dermatitis) treated with only systemic enzyme support was able to reduce skin itching manifestations, and in combination with basic conventional therapies it provided an marked acceleration of the desirable effects.

Urinary system condition improvement due to treatment with systemic enzyme support include a major improvement in relapsing urinary tract infections, decreased recurrence of kidney stones and decreased progression of diabetic nephropathy. There are also positive clinico-laboratory results, which considerably exceeded those in conventional drug treatment in patients with pyelonephritis.

Reproductive health, women’s health, men’s health and thyroid health conditions can all be more effectively managed by the use of systemic enzyme
support. It is an important part of the complex therapy of male and female sterility, recurrent miscarriages and chronic infections of the reproductive system. Systemic enzyme support is an effective immunomodulator for both autoimmune & alloimmune infertility.\textsuperscript{46-48} In women, it is effective for treatment in chronic pelvic inflammatory disease (PID) and as adjuvant in treatment of acute adnexitis.\textsuperscript{49-50} In men, systemic enzyme support is a very efficient therapy for both bacterial and abacterial prostatitis, as well as associated sexual dysfunction.\textsuperscript{51-53} Systemic enzyme support is also a very effective therapy for the management of fibrocystic breast disease and does not interfere with already upset hormonal balance.\textsuperscript{54-56} Autoimmune thyroid disease treated with systemic enzyme support resulted in a significant decrease of TSH, anti-TG & anti-TPO and allowed the lowering of L-thyroxine dosages.\textsuperscript{57} Joint health is profoundly improved by systemic enzyme support. It is an effective and safe alternative to NSAIDS in the treatment of painful episodes of osteoarthritis of the knee and hip.\textsuperscript{58-60} Systemic enzyme support protects and preserves joint cartilage significantly better than NSAIDs in rheumatoid arthritis.\textsuperscript{61-71} Gout therapies are significantly improved by the addition of systemic enzyme support.\textsuperscript{72} The addition of systemic enzyme support improved both articular signs and extra-articular manifestations in the majority of the children with juvenile chronic arthritis and was able to help limit the use of corticosteroids in some children. In addition to osteoarthritis, rheumatoid arthritis, gouty arthritides, and juvenile arthritis, systemic enzyme support has also been shown as effective in the treatment of psoriatic arthritis. It is fair to say that systemic enzyme support could be used in any form of arthritis. Sports medicine is another area in which systemic enzyme support excels. Sport & exercise related muscle pain & inflammation provoked by a strong physical tension, excessive training and heavy competition rate are decreased with "excellent results" due to the selective interferences of enzymes with the pathophysiologic mechanisms of exercise induced inflammation.\textsuperscript{73} A prophylactic administration of systemic enzyme support in top athletes who are at risk of injury results in significantly reduced duration of injury symptoms and in absence from training and work due to such injuries. Systemic enzyme support also improves recovery from sprains, as well as shortened recovery from sport injuries severe enough to also require surgery.\textsuperscript{74-77} 

**Biomarkers of Inflammation & Systemic Enzyme Support**

It is again important to note that the studies showing clinical efficacy in the aforementioned conditions are based on the enteric coated polypolyenzyme formulations which originated from Germany. Clinicians can be confident that they will observe the same degree of clinical efficacy with Wobenzym\textsuperscript{®} N, and Wobenzym\textsuperscript{®}PS, which are manufactured in Germany by that company. As well as the clinically observable benefits, systemic enzyme support improves the levels of a number of biomarkers of inflammation as mentioned above. Systemic enzyme support resulted in improvement or normalization in a number of biomarkers of inflammation. The decreased circulating immune complex (CIC) levels resulted in significant improvement in a wide range of conditions including rheumatoid arthritis, atherosclerosis, atopic dermatitis, Behçet's disease, chronic hepatitis, diabetes mellitus, and myocardial infarction.\textsuperscript{78-87} Decreased erythrocyte sedimentation rate was observed in urinary tract infections, adnexitis, rheumatoid arthritis, and surgical cases.\textsuperscript{88-93} Decreased C-
reactive protein (CRP) levels in lymphedema, rheumatoid arthritis, psoriatic arthritis and surgical cases was associated with improved clinical outcomes.\textsuperscript{94-96} The normalization of cytokine levels after tissue injury and inflammation was observed in rheumatoid arthritis and angina pectoris treated with systemic enzyme support.\textsuperscript{97-100} Normalization of immunoglobulins (IgG, IgE, IgA, IgM) is observable in treated cases of atopic dermatitis, recurrent infections of respiratory tract and rheumatoid arthritis.\textsuperscript{101-103} The restoration of normal fibrinolytic properties by systemic enzyme support is considered as vital for disease state management in rheumatology, immune complex diseases, traumatology, surgery, oncology, inflammations and vascular diseases as well as diseases with an infection component.\textsuperscript{104,105} Systemic enzyme support can also up-regulate amyloid beta catabolism and reduce the risk of developing Alzheimer’s disease by preventing amyloid beta accumulation in brain and vasculature.\textsuperscript{106-111}

**Clinical Conclusions**

Systemic enzyme support has been demonstrated to be an effective treatment either as the primary therapy, or as an adjuvant therapy which improves clinical outcomes of diseases which are difficult to manage. Systemic enzyme support has been reported to have excellent tolerance and superior safety when compared to some conventional therapies.\textsuperscript{112-116} The safety and efficacy of systemic enzyme support is coupled with a consumer loyalty rate of over 80 percent. This significant compliance to systemic enzyme support is believed to be primarily due to its effectiveness.

Published international literature describing the clinical efficacy of systemic enzyme support is based on formulations made by a German pharmaceutical company. Wobenzym\textsuperscript{®} N is manufacture by that same company, and available throughout the United States. Clinical observations and literature review both affirm the conviction that Wobenzym\textsuperscript{®} N is an essential component for successful management of inflammation disorders and other conditions with immune system dysregulation due to its high degree of clinical efficacy. More information can be found at [www.SystemicEnzymeSupport.org](http://www.SystemicEnzymeSupport.org), a non-commercial a health education and wellness promotion website dedicated to teaching the clinical efficacy of systemic enzyme support.

**References**


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No. 3/4, pp. 85-91.


