

## Inflammation

### What is Inflammation?

Inflammation is critical for our survival against a hostile world as it is our body's natural mechanisms to defend against a diverse variety of pathogens including bacteria, viruses, fungi, tumors and a number of various other harmful agents (chemicals, radiation, burns, and various wounds). Inflammation is a complex reaction of the body in response to cellular injury that is marked by tissue swelling, capillary dilation, anti-histamine activity, redness, heat and pain. It serves as a mechanism initiating the elimination of noxious agents and of damaged tissue.

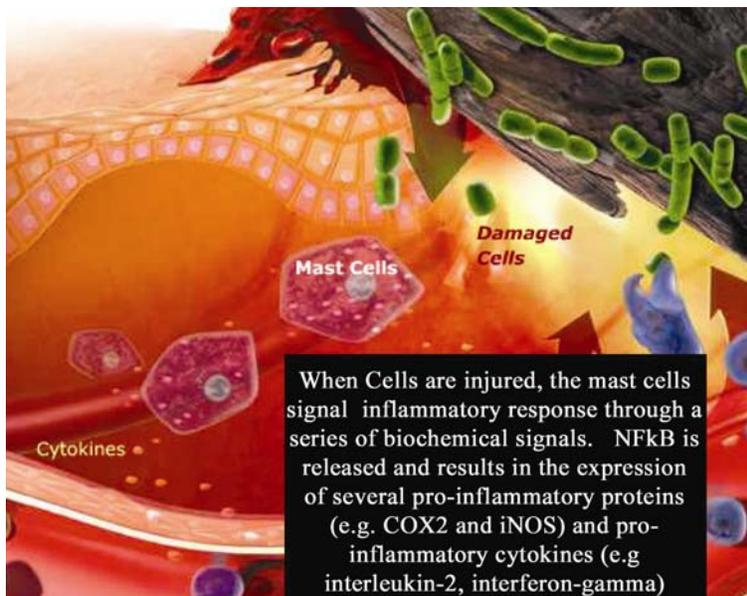
#### 5 Basic Symptoms of Inflammation

- Redness
- Swelling
- Heat
- Pain
- Deranged function.

#### Other "Flu"-like Symptoms

- Fever
- Chills
- Fatigue/loss of energy
- Headaches
- Loss of appetite
- Muscle stiffness

## Biochemistry of Inflammation



The damaged cell signals inflammatory response releasing NF kappa B, the key regulator to our inflammatory response system. These result in the expression of several pro-inflammatory proteins such as COX2 and iNOS that causes pain, fever, and swelling and heat of an affected area. Simultaneously, a series of pro-inflammatory cytokines such as interleukin-2, tumor necrosis factor-alpha, and interferon-gamma are released. (Cytokine is a group of proteins released by the cell in response to an antigen, a bacteria or virus.)



**Address:** 707 24<sup>th</sup> Avenue W

Bradenton, FL 34205

**Toll Free Tel** (877) 437-2234

**Toll Free Fax** (866) 278-2874

**Email:** [info@hpingredients.com](mailto:info@hpingredients.com)

**Web Site:** [www.hpingredients.com](http://www.hpingredients.com)

## Inflammation and Disease

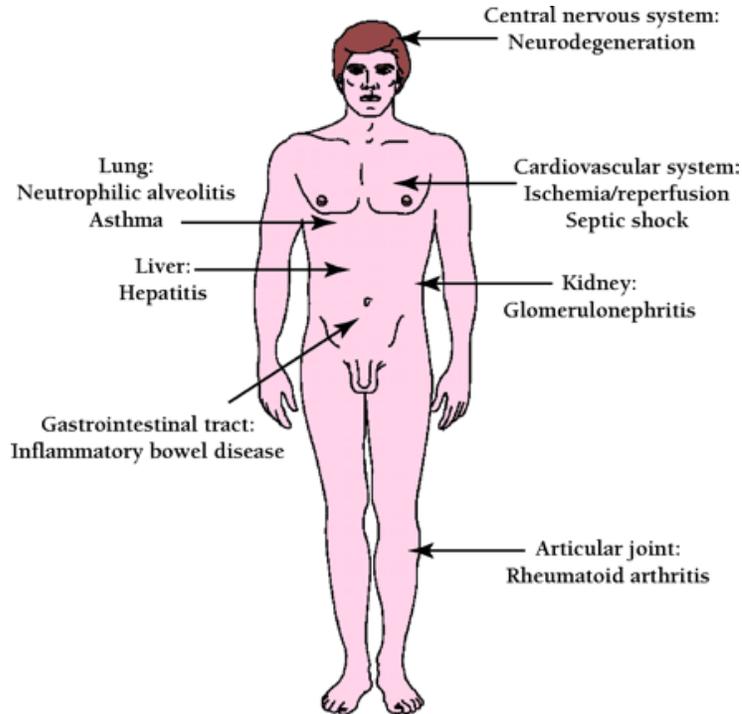
Inflammation is our primary host defense system. But researchers recognize inflammation as a key component of many of the major diseases affecting human health today. Inflammation contributes to disease by damaging the very tissues it has evolved to protect. Seemingly unrelated disorders such as asthma, Alzheimer, multiple sclerosis, inflammatory bowel diseases and rheumatoid arthritis all have common inflammatory elements that underlie the disease process.

**Classical inflammation** is usually associated with pain and can result from continuing wear of an overactive immune system that is constantly turned on so that the body attacks itself (rheumatoid arthritis, irritable bowel syndrome).

**Silent inflammation** happens when the immune system continues to attack at the cellular level (heart, immune system and brain) without the perception of pain. These continued insults often result in heart disease, cancer and Alzheimer.

### How it goes wrong?

In the process of destroying microorganisms, the inflammation response can also mistakenly affects healthy cells. Macrophages may start chewing up the cholesterol deposits in the coronary arteries, or glial cells begin destroying neurons in the brains. In other cases, inflammatory flares refuse to die down or are up for prolong period of time, causing autoimmune inflammation. After time, unchecked inflammatory response can lead to a number of serious conditions.



## Current Medications

To address this significant area of disease, pharmaceutical companies have developed numerous steroidal and non-steroidal anti-inflammatory drugs. The medications include:

- Non-steroidal anti-inflammatory drugs (NSAIDs - such as aspirin, ibuprofen or naproxen)
- Corticosteroids (such as prednisone)
- COX 2 inhibitors (Vioxx, Celebrex, Bextra)

### **The Danger of Pharmaceutical drugs**

Approximately 20,000 Americans die each year from the proper use of non-steroidal over-the-counter and prescription anti-inflammatory drugs. Aspirin and other NSAIDs decrease the production of PGs and thromboxane, thereby alleviating inflammation. However, long term use of NSAIDs can cause gastrointestinal side effects where many cases of ripping of stomach lining and bleeding has been reported.

COX2 inhibitors drugs were designed to block just the inflammatory functions of the COX-2 enzyme, leaving the stomach-protecting functions of the COX-1 form intact. In 2005, Vioxx, Celebrex and Bextra all showed an increased risk of heart problems in users. In separate studies published in the New England Journal of Medicine in Feb 2005, researchers found that high-dose

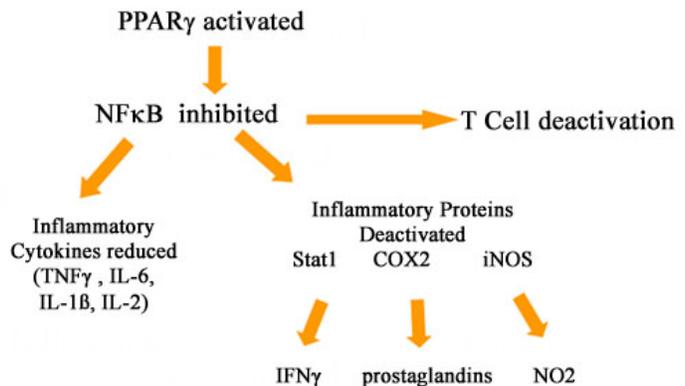
Celebrex users were three times as likely as nonusers to die from a heart or stroke event, while those taking Vioxx had twice the chance of suffering a heart attack or stroke.

## New Research on Treating Inflammation -- NFκB

Recent cellular and molecular mechanisms of inflammation have been the focus of designing new anti-inflammatory therapies. One of the most important inflammatory response mediators is NF-kappaB (NFκB), which is a critical activator of genes for inflammation and immunity. It plays a central role in regulating proinflammatory mediators (COX-2, iNOS) and proinflammatory cytokines (Interferon gamma, Interleukin 2, TNF alpha). Aspirin (salicylates) and glucocorticoids, two widely used NSAIDs, are now known to inhibit NFκB. Evidence from recent research demonstrates that by inhibiting NFκB, a wide range of diseases and conditions in which inflammation plays a critical role can be treated. Research now has shown that NFκB is activated in airway inflammation such as asthma and allergies. NFκB is also activated in rheumatoid synovium cells.

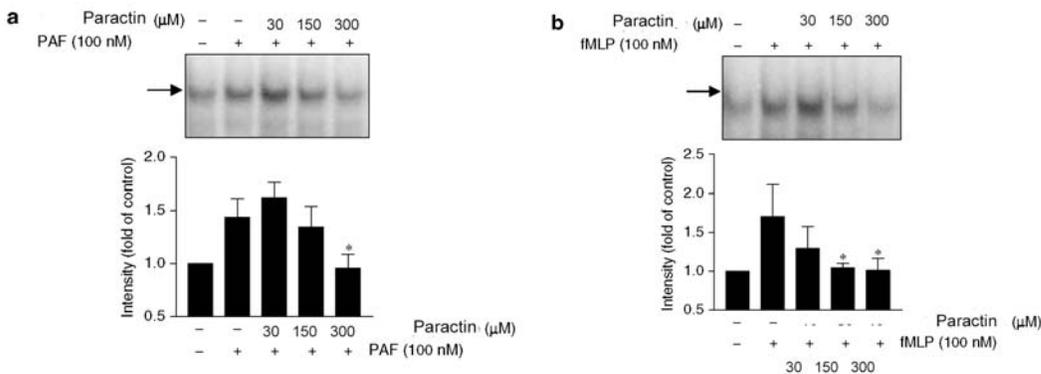
### What is ParActin®?

ParActin® is a patented extract of *Andrographis Paniculata*. Our research has shown ParActin® to naturally activate PPAR gamma, thereby inhibit NF kappa B, deactivate T cell proliferation, and reduce pro-inflammatory cytokines such as Interleukin 2, Interferon $\gamma$ , TNF  $\alpha$ , and COX 2.



### ParActin® Inhibits NF-kappaB

Both in vitro and in vivo research showed ParActin inhibited NF-κB activity and reduced significantly the DNA binding of NF-kappaB.



### ParActin® Reduces COX-2



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COX-2 is an enzyme responsible for inflammation and pain. COX-2 is induced in cells at sites of inflammation and converts arachidonic acid to prostaglandin. COX-2 is also regulated by NF- $\kappa$ B. In vitro research showed ParActin<sup>®</sup> inhibited the COX-2 expression and is a natural COX-2 inhibitor.

### ParActin<sup>®</sup> Reduces Pro-inflammatory Cytokines

**Interferons** play an important role in the first line of defense against viral infections. Interferon-gamma (immune interferon) is produced by certain activated T-cells and NK cells. Several autoimmune diseases such as multiple sclerosis, rheumatoid arthritis, psoriasis and diabetes, are associated with an increase level of IFN $\gamma$ .

**Interleukin-2 (IL-2)** is a protein produced by T-helper cells, a kind of white blood cell when stimulated by an infection. IL-2 makes infection-fighting cells multiply and mature. IL-2 can increase T-cell (CD4<sup>+</sup> cell) counts.

In vitro and in vivo research with ParActin<sup>®</sup> had shown ParActin<sup>®</sup> to effectively deactivate T cell proliferation, significantly reduce Interleukin 2 and Interferon gamma cytokines. In mice induced with MS, IL2, IFN $\gamma$ , and T cell return to normal after 20 days of treatment with ParActin<sup>®</sup>. The reduction in cytokine production explained the anti-inflammatory effect of ParActin<sup>®</sup>.

