

by Roger Clemens & Peter Pressman

Beyond Statins: Modulating Inflammation

Food and nutrition have long been discussed in the context of how certain dietary components may modulate oxidative stress or inflammation. The prospect of suppressing inflammation has been seen as a means of attacking one of the true “final common pathways” of the entire spectra of pathology. Whether it is aging, infection, cancer biology, or wound repair, inflammation remains central to the disease and healing processes.

There is growing evidence that the anti-inflammatory or immunomodulatory effects of the statin drugs (also known as HMG-CoA reductase inhibitors) such as *Lipitor*[®], *Zocor*[®], and *Mevacor*[®] may be at least as important therapeutically as their direct effect on decreasing plasma cholesterol and low-density lipoproteins to reduce the risk of myocardial infarction and stroke and retard the progression of atherosclerosis.

Thus, we increasingly face the need to rigorously define inflammation at the tissue and organ levels, delineate the role of inflammation in the physiology of both illness and health, and finally, and critically review what we know and what we need to know about nutrition, dietary components, and inflammation.

Inflammatory and anti-inflammatory processes are multifaceted and involve a cascade of biological events. In fact, inflammation protects the body against infection and injury

and participates in transient wound healing and tissue repair processes. For example, the inhibition of cyclooxygenase-2 (COX-2), an enzyme that is activated in inflammation and causes the presentation of inflammatory evidence—i.e., local heat, redness, swelling, pain, and altered function—is facilitated by non-steroidal anti-inflammatories (NSAIDs) such as *Celebrex*[®] and *Prexige*[®]. During the past two years, NSAIDs like *Vioxx*[®] and *Bextra*[®] have been

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withdrawn from the market because of increased gastrointestinal and cardiovascular risks.

While controversy and review continue even regarding the non-specific NSAIDs such as ibuprofen and naproxen, there is emerging evidence that statin drugs and dietary components may modulate the inflammatory processes. Statin drugs may reduce the incidence of ischemic stroke, probably through antithrombotic mechanisms, and reduce the symptoms of rheumatoid arthritis through proangiogenic effects on neovascularization leading to tissue repair.

Some dietary components may have similar effects. Twelve scientific, peer-reviewed publications since 1999 suggest that curcumin, the major yellow pigment in turmeric, curry, and

mustard, may potentiate apoptosis or inhibit growth of selected cancer cells and function as a COX-2 inhibitor in several in-vitro and animal models. The effects in mice and rats were observed with dietary curcumin from 0.05% to 2%. Topical or oral application of curcumin following chemically induced skin or liver cancer resulted in anti-carcinogenic effects.

Atherosclerosis, an inflammatory disease which may result from endothelial dysfunction,

may be modulated by a variety of dietary flavonoids through the inhibition of tumor necrosis factor alpha (TNF- α , also known as cachexin or cachectin) activity and expression, and possibly through the inhibition of nitric oxide production by macrophages. TNF- α , a cytokine involved in systemic inflammation, is released by white blood cells, endothelial cells, and several other tissues in the course of damage or insult.

Some metabolites of eicosapentaenoic acid (EPA), found in some fish oils, may inhibit several inflammatory control steps, such as the transcription of nuclear factor kappa B (NF- κ B), a pro-inflammatory factor found in all cell types, and thus prevent the activation of inflammatory genes and block the terminal

stages of arachidonic acid synthesis from its precursors. There is preliminary in-vitro evidence that extracts of some herbs, such as the stinging nettle (*Urtica dioica*) and cat's claw (*Uncaria tomentosa*), may function as COX-2 inhibitors.

These are interesting observations that require clinical evaluation, development of appropriate biomarkers, determination of dose–effect relationships, and certainly regulatory guidance. In addition, advances in bioactive dietary components require development of validated chemical analysis tools and procedures for the identification and quantification of these substances.

Enhanced understanding of these aspects of dietary components and inflammatory processes may expand our understanding of acute and chronic pathologies and health-modulating processes, and lead to the development of foods and food systems which will present fewer contraindications than are experienced with the use of some pharmaceutical products. **FT**



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