THE ROLE OF INFLAMMATION IN HEALTH AND DISEASE
By Elvira Gonzalez de Mejia, PhD

Chronic inflammation has been related to diseases such as cardiovascular disease, bone disease, muscular dystrophy, osteoporosis, neurological disorders such as Alzheimer and Parkinson; metabolic complications like type-2 diabetes and obesity; chronic renal failure and sepsis; and to different types of malignancies such as colon, pancreatic and lung cancer.1-5 During chronic inflammation mediated diseases, macrophages produce certain markers that exacerbate the syndrome. Thus, inflammation can be measured by the use of different markers such as interleukins (IL), nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB), tumor necrosis factor-α (TNF-α), cyclooxygenases (COX) and nitric oxide (NO) among others. NF-κB induces the transcription of proinflammatory mediators, such as inducible nitric oxide synthase (iNOS), COX-2, TNF-α and (IL)-1β, -6 and -8.6-8 During the inflammatory process, large amounts of proinflammatory mediators, like NO and prostaglandin E2 (PGE-2) are generated by iNOS and COX-2, respectively. iNOS is expressed in response to interferon-γ (IFN-γ), lipopolysaccharide (LPS) and a variety of proinflammatory cytokines.9 COX-2 converts arachidonic acid to prostaglandins during the inflammatory process.10

Environmental signals also modulate NF-κB which regulates the transcription of several genes involved in the inflammatory immune response. At the molecular level, TNF-α and IL-1β are critical in initiating the inflammatory response by binding to their receptors and activating NF-κB pathways.2 Osawa et al.11 have indicated that persistent infection, immune-mediated inflammatory disease, or prolonged exposure to toxic reagents results in persistent accumulation and activation of leukocytes that cause chronic inflammation. The NF-κB proteins are localized in the cytosol of the cell and are bound to inhibitory proteins known as inhibitor of κB (IκB). The IκB proteins are normally bound to

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NF-κB sub units, p50 and p65, and block their nuclear localization signal. If the inhibitor of κB kinase (IκK) is activated through stimuli, NF-κB subunits are released and translocate to the nucleus inducing inflammatory pathways and consequently promoting inflammatory-associated diseases, therefore therapeutic strategies might directly target and inhibit NF-κB signaling pathways.

**Soy Protein and Inflammation Reduction**

Bioactive peptides are released from dietary proteins through gastrointestinal hydrolysis and also during protein hydrolysis and fermentation. In addition to providing essential amino acids for a variety of systemic modulatory pathways, proteins and peptides may also elicit anti-cancer, anti-microbial, hypocholesterolemic, anti-hypertensive, anti-thrombotic and anti-inflammatory effects. It has been found that dietary proteins and peptides can regulate pathways in the cardiovascular disease process (CVD) due to their role as antioxidants, anti-inflammatory, antithrombotic, antihypercholesterolemic, and antihypertensive among other properties.

Soybeans (Glycine max) contains more than 40% protein in dry weight. In the U.S., production and consumer demand for soy products increased significantly after the Food and Drug Administration approved in 1999 the claim that 25 g of soy protein a day, as part of a diet low in saturated fat and cholesterol, may reduce the risk of heart disease. There are several products commercially available that contain soybean proteins such as edamame, miso, soymilk, soy yogurt; tempeh and tofu. Also, soy protein isolate and concentrate are available as ingredients to be incorporated into a variety of processed foods. The results of these studies have indicated that the consumption of soy may reduce cardiovascular risk factors such as low-density lipoprotein (LDL), cholesterol and blood triglycerides and increase high-density lipoprotein (HDL) cholesterol. These studies have largely been conducted on food products containing whole soy, which also contain vitamins, minerals, isoflavones and other bioactives aside from protein. A meta-analysis conducted on the effect of soy protein supplementation found statistically significant reductions on serum lipids in studies in which high amounts of soy protein were consumed (20 to > 61 g/day). In this meta-analysis, phytochemicals associated with soy protein primarily comprised phytoestrogens. Effective doses were reported from 37.5 mg aglycone units/day to 62 mg isoflavones. Therefore, more recent investigations on soy protein supplementation would determine the direct impact of soy protein on inflammation and CVD risk factors.

Soy protein has been studied due to its potential to mitigate risk factors associated with cardiovascular disease, and numerous epidemiological and clinical studies have been performed.

Specific bioactive peptides naturally present in soy such as lunasin, which is a 43-amino acid component with a unique arginine-glycine-aspartic acid cell adhesion motif and polyaspartic acid sequence have also been studied. In my laboratory, we have found, that lunasin inhibits proinflammatory cytokines IL-1B, IL-6, cyclooxygenase-2, nitric oxidation production, inducible nitric oxide synthase expression and prostaglandin E-2 through suppression of NF-κB in RAW 264.7 murine macrophages. As a result, lunasin may have a therapeutic effect on CVD risk by preventing the activation of the inflammatory cascade and uncontrolled inflammation by macrophages in atherosclerotic lesions. Dia et al. demonstrated the bioavailability of lunasin in humans after healthy men consumed 50 g of soy protein for 5 days. Thus, lunasin possesses promising potential in the prevention of CVD due to its anti-inflammatory effects and post-prandial biological stability. In addition to lunasin, other bioactive peptides derived from soybeans have been shown to upregulate LDL receptor levels. Several animals and human studies have demonstrated potential anti-inflammatory effect associated to the consumption of soybean and its derivatives. The beneficial effects are attributed to bioactive compounds such as isoflavones, saponins, lunasin, and peptides obtained from soybean enzymatic hydrolysis. Other studies have demonstrated the anti-inflammatory and antioxidant properties of soy hydrolysates. Kong et al. showed that the hydrolysates produced by alcalase enzyme when compared with other enzymes showed a higher...
A can of soybeans makes this spice cake extra moist.

1 can (15 oz.) soybeans
1 package (18.25 ounces) spice cake mix
Oil, water, and eggs according to package directions
Canned frosting (optional)

Method of Preparation:
1. Preheat the oven as called for on the cake package and prepare the baking pan.
2. Rinse the soybeans under warm water and drain them well. Put them in a blender with about one-half cup of the water called for on the package. Purée until smooth, one to two minutes. If necessary, add a little more of the water to the blender.
3. Put the cake mix, oil, remaining water, eggs, and puréed soybeans into a large mixing bowl. Beat according to package directions. Pour the mixture into the prepared pan and bake as specified on the package. Baking times should be approximately the same as on the package, maybe slightly longer.
4. Remove the cake from the oven and let cool. Frost as desired.

Nutritional Analysis: Per serving | Calories 140, Fat 6g (1g saturated), Protein 4g, Carbohydrate 19g, Sodium 170mg

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Dietary consumption of soy protein may be beneficial in reducing inflammation and inflammatory-related diseases.

Complementary/alternative therapies, such as the consumption of soy proteins, may be helpful in regulating pro-inflammatory cytokines/chemokine activity in inflammatory-related diseases.

Ongoing experiments and clinical trials should continue in order to guide and provide scientifically based effectiveness information to reduce inflammation and promote wellness.

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ABOUT THE AUTHOR

Elvira de Mejia has a BS in Biochemical Engineering, MS in Food Science and Technology and PhD in Plant Biotechnology. She joined the University of Illinois in 2002 and she is currently an Associate Professor in the department of Food Science and Human Nutrition. Her research has been published in the Journal of Agricultural and Food Chemistry of the American Chemical Society, as well as in the Analytical Chemistry, Food and Chemical toxicology, Food Chemistry of the British Chemical Society, Molecular Nutrition and Food Research, Peptide, Cancer Letters and others.

Complete references for this article can be found at www.soyconnection.com
The widespread use of vegetable oils, particularly soy oil, for commercial food production as well as cooking in the home resulted in a dramatic rise in linoleic acid (LA) intake over the last five decades. LA intake in much of the Western world has been estimated at 15 to 20 grams per day per person, and may account for up to 10 percent of a person’s daily calorie intake.1 A large body of evidence supports the conclusion that diets rich in LA reduce the risk of cardiovascular disease. However, a few prominent researchers believe that current intake levels of LA are too high and contribute to the development of numerous chronic diseases, in large part, by promoting inflammation.2-3 As a result, some health professionals are recommending that LA intake should be greatly reduced. This article introduces the reader to a representative sampling of the scientific evidence which supports the conclusion that LA intake at current levels is safe and does not appear to promote inflammation in normal, healthy people.

Surprisingly, there are a limited number of studies that directly address the question of whether dietary fats rich in LA affect the inflammatory status of humans. Recently the author, along with a nutritional science expert and colleague, Guy Johnson, completed an evidence-based review of all the scientific literature related to this issue. While space limitations prevent a presentation of all the pertinent studies, the results from a few representative studies will be described in brief.

There are numerous biomarkers of inflammation that have been used in human studies. However, no consensus exists regarding which biomarker is best, since each has advantages and disadvantages. As a result most researchers measure multiple biomarkers of inflammation in the hope that one or more of them will have predictive value in changes in clinical outcomes.

In 2003, Pischon and coworkers4 examined the relationship between habitual intake of LA and alpha-linolenic acid (ALA), an omega-3 (n-3) polyunsaturated fatty acid (PUFA), and inflammatory markers in over 50,000 male health professionals aged 40 to 75 years. The two key conclusions that emerged from this study were: 1) high intakes of both LA and n-3 PUFA were associated with the lowest levels of inflammation; and 2) consumption of LA did not inhibit the modest anti-inflammatory effects of n-3 fatty acids.

In one of the more comprehensive studies of its kind, Ferrucci, et al.5 examined the relationship of plasma PUFA to circulating inflammatory markers in humans. In this epidemiological study, blood samples were obtained from nearly 1,300 men and women from two small towns in the Tuscany area of Italy. After adjusting for age and other confounders, the authors found several significant associations between total n-6 and n-3 PUFA and various pro- and anti-inflammatory markers. The authors reported that when total n-6 or n-3 PUFA were grouped into quartiles, those individuals in the lowest quartile of plasma total n-6 PUFA had the highest levels of tumor necrosis factor-alpha (TNF-α) and interleukin-6 (i.e., pro-inflammatory markers) and the lowest levels of anti-inflammatory markers (i.e., IL-10 and TGF-β).

Finally, Liou, et al.6 purposely reduced LA intake in 22 healthy individuals to determine if this type of intervention would reduce signs of inflammation. LA intake was reduced from 12% of total calories down to 4%, while maintaining a constant intake of n-3 PUFA (i.e., 1% of total energy as ALA). After 4 weeks on the low LA diet, the circulating levels of interleukin-6 and C-reactive protein, two frequently used markers of inflammation, were unchanged.

In summary, the results described here, as well as all of the other currently available evidence, fail to show a link between high dietary LA intake and greater inflammation in humans. These data are contradictory to numerous animal-based studies that show a link between dietary LA and inflammatory disease. Space limitations prevent the inclusion of the many possible explanations for why studies in animals may not reflect what happens in people. Regardless of the reasons for these paradoxical findings, current dietary recommendations that promote the intake of both n-6 and n-3 PUFA (from sources such as soybean and canola oils) appear to be justified and appropriate for most consumers.

ABOUT THE AUTHOR

Kevin L. Fritsche, PhD, is a professor of nutrition and immunology in the Division of Animal Sciences and Program Leader for the Food-for-the-21st Century Nutrition for Health Group at the University of Missouri. He received his PhD in nutritional biochemistry from the University of Illinois in Champaign/Urbana in 1988. For the last 23 years or so, his research program has been investigating the impact of fatty acids on the immune system. He has published several reviews on the topic of fatty acids and health.
“Consume less than 10 percent of calories from saturated fatty acids (SFA) by replacing them with monounsaturated (MUFA) and polyunsaturated fatty acids (PUFA).” This statement is the current recommendation for SFA from the 2010 Dietary Guidelines. The Dietary Guidelines for Americans provides science-based advice to promote health and reduce the risk of major chronic diseases.

To limit consumption of the major sources of foods high in SFA, consumers are encouraged to replace them with foods that are rich in MUFA and PUFA. For example, solid fats (e.g., butter and lard) can be replaced with liquid vegetable oils. Some of these oils are rich in MUFA such as canola, olive, and safflower oils. Others are good sources of PUFA and include soybean, corn, and cottonseed oils (see Figure 1). Sunflower oil can be a rich source of PUFA (see Figure 1) but is often manufactured and sold as “high oleic” (or high MUFA), which can be a source of confusion for consumers.

Current dietary guidance recommends that PUFA provide 5% to 10% of energy. Current intake of PUFA in the US is 7% of energy, which includes both omega-6 and omega-3 fatty acids. The predominant fatty acid in the diet is the omega-6 fatty acid linoleic acid, which comprises about 90% of total dietary PUFA. A 2000 calorie diet with 5–10% of energy from PUFA provides 10 to 21 g. Consumption of PUFA is approximately 17 g per day, of which about 15 g is from omega-6 fatty acids (predominantly linoleic acid); the remaining 2 grams come from plant-derived and marine omega-3 fatty acids.

The major food sources that contribute to PUFA intake are shown in Table 1 (see page 6). Many of the foods listed also are major sources of SFA. For example, of the top 10 food sources of PUFA, seven are major sources of SFA. These include chicken and chicken mixed dishes; grain-based desserts; potato/corn/other chips; pizza; pasta and pasta dishes; fried white potatoes and Mexican mixed dishes. Since SFA intake in the U.S. is 11% of energy (NHANES, 2005–2006), which exceeds recommended guidelines, a focus should be on decreasing SFA while continuing to


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Soy Oil Good Substitute for Solid Fat Source of SFA  

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Tips for Practice

Thus, low SFA, high PUFA foods should be incorporated into the diet as substitutes for foods high in both SFA and PUFA. A simple and routinely implemented strategy to achieve this is to decrease solid fat sources of SFA in the diet and replace them with vegetable oils—particularly those high in PUFA. Using soybean oil, which is high in PUFA and low in SFA, in salad dressings and vegetable stir fry’s are strategies for incorporating PUFA in the diet without increasing SFA. Other strategies include simple food substitutions. For example, replacing butter or cream cheese on a bagel with a high PUFA margarine or replacing cheese on salads with nuts or seeds will decrease SFA and increase PUFA without changing total fat or calories. Through simple substitutions, achieving the standards of a lower fat, low saturated fat diet containing optimal amounts of PUFA’s can be easy.

Table 1. Food sources of total n-6 fatty acids by percent contribution to intake based on National Health and Nutrition Examination Survey, 2005-2006.

<table>
<thead>
<tr>
<th>Food Item</th>
<th>Contribution to intake %</th>
<th>Cumulative contribution %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chicken and chicken mixed dishes</td>
<td>9.5</td>
<td>9.5</td>
</tr>
<tr>
<td>Grain-based desserts</td>
<td>7.4</td>
<td>16.9</td>
</tr>
<tr>
<td>Salad dressing</td>
<td>7.3</td>
<td>24.3</td>
</tr>
<tr>
<td>Potato/corn/other chips</td>
<td>6.9</td>
<td>31.2</td>
</tr>
<tr>
<td>Nuts/seeds and nut/seed mixed dishes</td>
<td>6.4</td>
<td>37.6</td>
</tr>
<tr>
<td>Pizza</td>
<td>5.3</td>
<td>42.9</td>
</tr>
<tr>
<td>Yeast breads</td>
<td>4.5</td>
<td>47.4</td>
</tr>
<tr>
<td>Pasta and pasta dishes</td>
<td>3.5</td>
<td>54.4</td>
</tr>
<tr>
<td>Fried white potatoes</td>
<td>3.5</td>
<td>50.9</td>
</tr>
<tr>
<td>Mexican mixed dishes</td>
<td>3.3</td>
<td>57.7</td>
</tr>
<tr>
<td>Mayonnaise</td>
<td>3.1</td>
<td>60.8</td>
</tr>
<tr>
<td>Quickbreads</td>
<td>3.0</td>
<td>63.8</td>
</tr>
<tr>
<td>Eggs and egg mixed dishes</td>
<td>2.9</td>
<td>66.7</td>
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<tr>
<td>Popcorn</td>
<td>2.6</td>
<td>69.2</td>
</tr>
<tr>
<td>Sausage, franks, bacon, and ribs</td>
<td>2.1</td>
<td>71.4</td>
</tr>
</tbody>
</table>

ABOUT THE AUTHORS

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Complete references for articles in The Soy Connection can be found at www.soyconnection.com
REFERENCES

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