*Invited Review*

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# Anti-Inflammatory Diet in Clinical Practice: A Review

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**Mari Anoushka Ricker, MD[1]; and William Christian Haas, MD, MBA[1]**

**Abstract**

Recently, there has been an increase in the research regarding the impact of acute and chronic inflammation on health and disease. Specific foods are now known to exert strong effects on inflammatory pathways within the body. Carefully selecting foods that are anti-inflammatory in nature while avoiding foods that are proinflammatory is central to an anti-inflammatory diet plan. Ultimately, the plan models a pattern of eating that (1) focuses on eating whole, plant-based foods that are rich in healthy fats and phytonutrients and (2) maintains a stable glycemic response. (*Nutr Clin Pract*. 2017;32:318-325)

**Keywords**

anti-inflammatory diet; fatty acids; Mediterranean diet; glycemic index; nutrition therapy

Inflammation is one of the many responses of the immune system used to defend the body from injury. Classically, inflammation has been defined according to the effects of capillary dilatation and leukocyte infiltration, causing redness, heat, pain, and swelling.[1] From an evolutionary standpoint, the inflammatory response is inherently protective, eliminating destructive agents and healing damaged tissue in a temporary, self-limiting manner. However, when noxious stimuli persistently confront the body and/or the inflammatory response fails to resolve, chronic inflammation ensues.

Unlike acute inflammation, chronic inflammation is often indolent, causing silent damage systemically throughout the body. The clinically used markers of acute inflammation (erythrocyte sedimentation rate, C-reactive protein [CRP]) may not be elevated in the early stages of low-grade inflammation.

Over time, as organ damage increases, chronic diseases become apparent. Several disease states have now been associated with chronic inflammation: diabetes mellitus, coronary artery disease, and asthma.[2-4] Although inflammation is not the sole factor driving these disorders, it is a process that is strongly influenced by nonpharmaceutical interventions, such as diet. The following review evaluates the effect of various foods on the inflammatory response, and it outlines key components of an anti-inflammatory diet plan.

## Nutrient Effects on Inflammation

### *Carbohydrates*

One of the primary dietary factors affecting inflammation is the consumption of refined, high glycemic–load carbohydrates. Glycemic load is defined as the quantity of carbohydrate ingested, multiplied by the rate at which that carbohydrate enters the bloodstream (ie, the glycemic index). Regular consumption of high glycemic–load carbohydrates results in chronic hyperglycemia, which, through varying mechanisms, increases the production of free radicals and proinflammatory cytokines.[5,6] In attempt to reduce elevations of blood glucose, the pancreas secretes insulin. Aside from shuttling glucose out of the bloodstream, insulin exerts influence on the enzymes delta-6 and delta-5 desaturase, rate-limiting enzymes controlling the conversion of linoleic acid into arachidonic acid.[7,8] Hence, the greater the insulin response to high glycemic–load carbohydrates, the more arachidonic acid produced. Of note, glucagon exerts an inhibitory effect on the desaturase enzymes, thereby reducing the production of arachidonic acid.[8]

### *Fats*

Another important dietary contributor to inflammation is the level of ω-3 and ω-6 fatty acids (FAs) consumed. In general, ω-3 FAs are considered anti-inflammatory, while ω-6 FAs are proinflammatory. However, both FAs are essential nutrients within the body, and it is the ratio of these FAs that likely determines inflammation levels.[9] Although the precise ratio promoting inflammation is unknown, a ratio of ω-6:ω-3 FAs >10:1 is believed to be proinflammatory, which is likely 10-fold higher than the ratio that humans evolved eating.[10,11] Several studies, in fact, have demonstrated

From the [1]Center for Integrative Medicine, Department of Family and Community Medicine, University of Arizona, Tucson, Arizona, USA.

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**Corresponding Author:**
Mari Anoushka Ricker, MD, Center for Integrative Medicine, Department of Family and Community Medicine, University of Arizona, PO Box 245153, Tucson, AZ 85724-5153, USA.
Email: rickerm@email.arizona.edu

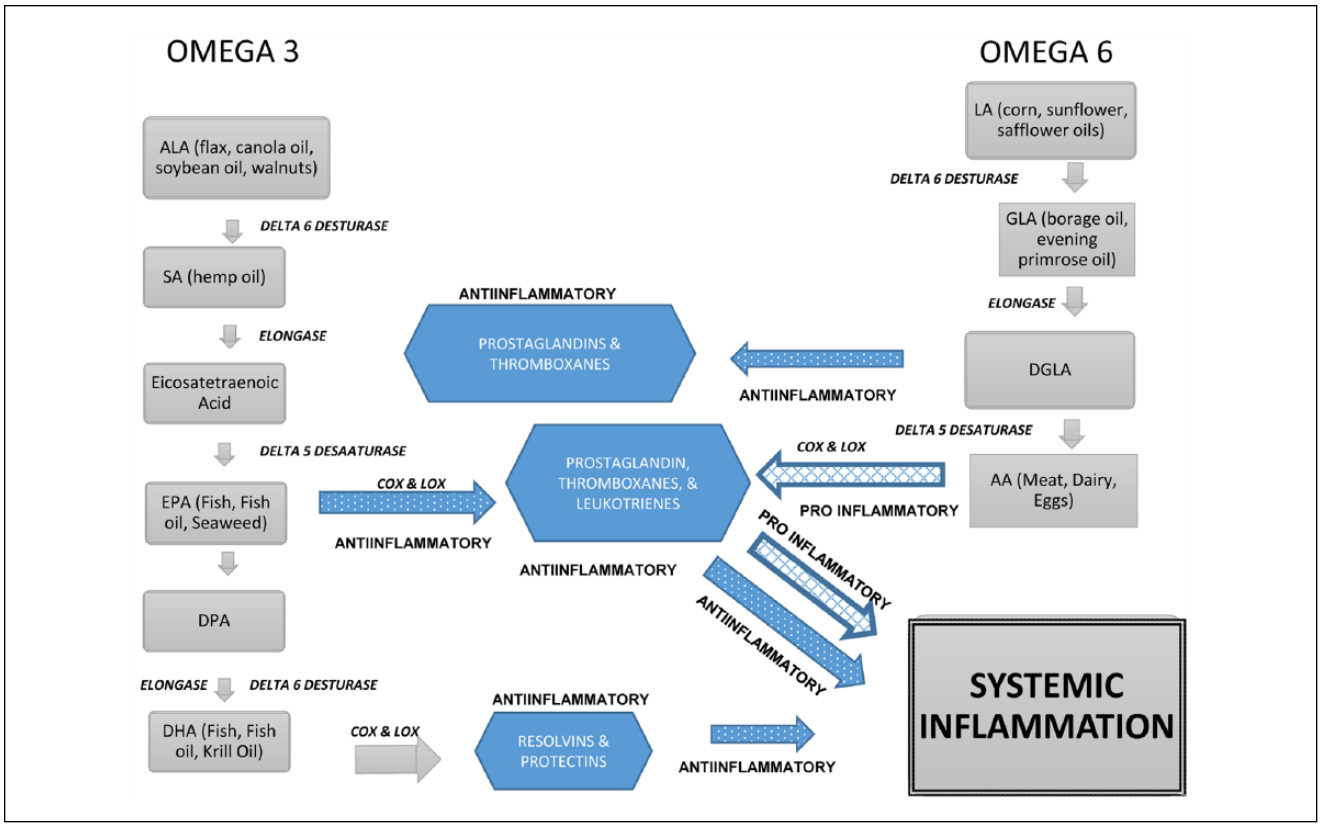


**Figure 1.** Fatty acid effects on systemic inflammation. AA, arachidonic acid; ALA, alpha-linolenic acid; COX, cyclooxygenase; DGLA, dihomo-gamma-linoleic acid; DHA, docosahexaenoic acid; DPA, docosapentaenoic acid; EPA, eicosapentaenoic acid; GLA, gamma-linoleic acid; LA, linoleic acid; LOX, lipoxygenase; SA, stearidonic acid.

a positive impact on various disease states (cardiovascular disease, rheumatoid arthritis, asthma) when the ω-6:ω-3 FAs ratio drops <5:1.[12]

A closer look at the metabolism of ω-6 and ω-3 FAs clarifies their effect on the inflammatory process (Figure 1). Linoleic acid, an ω-6 FA, serves as the precursor for a number of proinflammatory eicosanoids produced from arachidonic acid. As a result, the more ω-6 FAs consumed in the diet, the greater the propensity for increased levels of inflammation. ω-3 FAs, however, exert a number of anti-inflammatory effects. Opposite to the effect of insulin, ω-3 FAs inhibit the delta-6 desaturase enzyme, reducing the production of arachidonic acid in the first place.[8] Once arachidonic acid is produced, though, ω-3 FAs can indirectly limit the generation of proinflammatory eicosanoids by competing with arachidonic acid for space in the phospholipid bilayer of cell membranes.[13] Finally, ω-3 FAs can defuse existing inflammation by contributing to the production of a class of anti-inflammatory eicosanoids known as resolvins, which are believed to regulate activation and trafficking of polymorphonuclear leukocytes.[14,15]

In addition to the level of polyunsaturated fats consumed, trans FAs (TFAs) in the diet have a strong impact on inflammation. Present in small amounts of meat and dairy products from ruminant animals, TFAs are primarily consumed in foods prepared with partially hydrogenated vegetable oils (eg, bakery goods). The process of hydrogenation converts naturally occurring *cis* double bonds of unsaturated fats to trans double bonds, thereby producing a long-lasting solid fat with a high melting temperature. TFA consumption has well-established adverse effects on serum lipids, primarily due to the modulation of liver function and the metabolism of liporprotein.[16,17] However, evidence also suggests TFAs to be inherently proinflammatory. In clinical trials and observational studies, TFA consumption has been associated with increased markers of systemic inflammation, including tumor necrosis factor (TNF), CRP, and interleukin 6.[16,18,19] Moreover, TFAs may impair the metabolism of essential FAs involved in inflammatory pathways.[20]

## *Polyphenols*

The shift away from freshly prepared foods to processed foods has reduced the consumption of plant-based phytochemicals, such as polyphenols. Although polyphenols are not considered an essential nutrient, mounting evidence suggests that they are

an important contributor to optimal health, partly through a reduction of inflammation.[21-23] The anti-inflammatory effect of polyphenols was initially attributed to their ability to neutralize free radicals, resulting from their structure of conjugated double bonds with a free hydroxyl group. Polyphenolic compounds may also increase endogenous antioxidant defense through the regulation of Nrf2, an important cellular redox transcription factor involved in phase 2 detoxification.[24] Beyond their antioxidant effects, polyphenols dampen the inflammatory response. Polyphenols activate gene transcription factors that inhibit the activation of NF-kB, an important transcription factor responsible for activating inflammation pathways.[25]

### *Caloric Intake*

Beyond the impact of specific nutrient groups, chronic inflammation is affected by caloric intake. Excess caloric intake, particularly in sedentary individuals, results in increased adiposity. Adipose tissue is a metabolic active tissue that directly contributes to chronic inflammation through the release of proinflammatory cytokines, including TNF-α and interleukin 6.[26] As adipocytes enlarge, further inflammation ensues as a result of infiltration and activation of macrophages that release additional inflammatory cytokines.[27] A number of other proinflammatory alterations occur as a result of excess adipose tissue, including increased insulin resistance and sympathetic nervous system activation.[28,29]

In contrast to excess caloric consumption, calorie restriction with adequate nutrition intake has been shown to exhibit important anti-inflammatory effects. Reducing the number of adipocytes in the body through calorie restriction lowers the level of proinflammatory adipokines and cytokines.[30] The same reduction of fat cells also improves insulin sensitivity and reduces plasma glucose levels, thereby lowering the production of advanced glycation end products. The reduction of advanced glycation end products dampens the activation of pathways that would otherwise promote expression of adhesion molecules and chemokines, induce oxidative stress, and release inflammatory cytokines and growth factors.[31] Separate from its effects on adipose tissue, calorie restriction enhances endogenous corticosteroid production, promoting anti-inflammatory effects in the body.[32] Finally, calorie restriction may increase parasympathetic tone, contributing to the suppression of cytokine-mediated inflammation.[33]

## Anti-Inflammatory Diet

Despite a growing awareness for the health benefits of an anti-inflammatory diet, a single universal definition does not exist. One of the first versions of an anti-inflammatory diet was published in 1995 in *The Zone Diet*, by Barry Sears, PhD.[34] The concept of designated macronutrient ratios and their impact on cortisol and insulin levels were key to his definition. In recent research, the Mediterranean and Okinawan diets have been identified as dietary patterns with anti-inflammatory properties.[35-37] As a result, the most commonly used definition of an anti-inflammatory diet currently incorporates aspects of both the Mediterranean diet and the Okinawan diet, in addition to recommendations for balancing macronutrient ratios. Beyond outlining a general dietary pattern, an anti-inflammatory diet incorporates the use of herbs, spices, and supplements that complement the overall dietary approach.[38-40]

The standard American diet provides a stark contrast to the beneficial components of an anti-inflammatory diet. Most Americans eat more red meat, less fish, more sugar and simple carbohydrates, and fewer fruits and vegetables than are included in the Mediterranean and Okinawa diets.[41] The Mediterranean diet, eaten by those living near the Mediterranean Sea, is high in vegetables, fruits, fish, and olive oil and includes moderate red wine intake.[36,37] The Okinawa diet, named after the southernmost Japanese prefecture, is also high in vegetable and fruit intake and lacking in dairy and red meat. In contrast to the Mediterranean diet, however, the Okinawan diet is much lower in overall fat intake[35] (see Table 1).

### *Vegetables and Fruits*

An anti-inflammatory diet relies on vegetables and fruits to make up a large portion of the diet. Vegetables and fruits are lower in caloric density and abundant in beneficial nutrients, including vitamins, minerals, and phytonutrients. Generally, they should be eaten in large volumes, with every meal, and in a variety of colors and types. Vegetables and fruits contain large concentrations of polyphenols, giving them their characteristic colors yet, more important, providing their anti-inflammatory properties. Moreover, fruits and vegetables, especially the non-starchy varieties, are high in fiber, reducing their glycemic index relative to other carbohydrates.[39] An ideal anti-inflammatory diet should ultimately contain up to two-thirds of the total food volume in vegetables and fruits.[39] As discussed, many studies have shown that diets high in fruits and vegetables correlate with lower levels of inflammatory markers in the blood.[42,43]

In practice, an anti-inflammatory diet emphasizes eating more vegetables than fruits, due to the lower glycemic index of the former. Whenever possible, vegetables should be organic in variety, as they are lower in pesticides and possess higher levels of antioxidants than the conventional variety.[44] Additionally, efforts should be made to eat vegetables and fruits in season, when they are fresh, yielding more available nutrients and, thus, antioxidant properties, often at a cheaper cost. Many fruits and vegetables, however, retain and even enhance their nutrients when frozen, providing a good alternative when eaten out of season, as they are picked at peak ripeness. Most fruits and vegetables are then blanched and frozen immediately.[45] Vegetables can be easily prepared with small amounts of olive oil and anti-inflammatory spices (discussed later).

### *Protein Sources*

Protein in an anti-inflammatory diet should be primarily plant based, with some sources of fish and small amounts of lean

**Table 1.** Comparison of Diet Components.

| Diet | Standard American Diet | Mediterranean Diet | Okinawan Diet | Anti-Inflammatory Diet |
|---|---|---|---|---|
| Vegetables and fruits | Fewer vegetables | High consumption of vegetables and fruits | High consumption of vegetables: orange-yellow root vegetables, leafy green vegetables | High consumption of vegetables: large diversity, including variety of colors to increase phytonutrients |
| Protein source | Red meat | Fish | High consumption of legumes (soy) | Plant sources of protein: legumes, soy, nuts, and seeds |
| | Dairy | Legumes | Small to moderate amounts of fish | More fatty fish and some lean animal protein |
| | | Nuts | Less meat | |
| Carbohydrates | Refined carbohydrates; high-fructose corn syrup and added sugar<br>Fewer whole grains | Whole grains | Small amounts of rice and noodles<br>Less sugar and fewer refined grains | Whole grains in small amounts, high fiber, reduced refined carbohydrates |
| Dairy | High-fat dairy sources | Low-fat dairy, such as yogurt | Less dairy | |
| Fats | Solid added fats, such as butter and sour cream | Olive oil as source of added fat | Lower fat overall | Olive oil for added fat source |
| Other features | Soda and added-sugar beverages | Moderate red wine intake | Moderate alcohol intake, green tea intake; broth-based soups | Spices: turmeric, garlic, ginger, and other anti-inflammatory herbs and spices |
| Cultural | Eating on the run, overeating | Highly social and connected eating experiences | Low caloric diet; highly ritualistic culture | Mindful eating approach; quality over quantity |

natural meats.[46] The type of fat contained within the protein source is a central determinate in whether it is anti-inflammatory versus proinflammatory. Animal protein contains higher levels of ω-6 FAs, and an anti-inflammatory diet should include protein sources containing higher levels of ω-3 FAs.[47] When consuming animal protein, one should eat fresh-water fatty fish containing high levels of ω-3 FAs, including salmon, mackerel, halibut, sardines, and herring. Careful attention should be given to sourcing wild-caught fish while avoiding farm-raised fish, as wild-caught fish have higher levels of ω-3 FAs.[48,49] As with fish selection, beef produced from naturally grazing cattle have lower ω-6:ω-3 ratios as compared with conventional beef.[50] In addition to grass-feeding practices, organically produced dairy and meats have been shown to contain higher levels of anti-inflammatory ω-3 FAs versus their nonorganic counterparts.[51] Another important aspect of meat consumption includes the cooking method. Meats cooked at high temperature or charred produce heterocyclic amines and polycyclic aromatic hydrocarbons and create advanced glycation end products,[52,53] which are proinflammatory. Furthermore, the heterocyclic amines and polycyclic aromatic hydrocarbons have been shown to be mutagenic and to cause cancer in animal models.[54] Although a direct link to cancer has not been established in humans, epidemiologic studies have found strong associations with cancer among individuals consuming large amounts of meat cooked well-done or grilled.[55-57]

Although an anti-inflammatory diet permits the intake of some animal protein, plant-based proteins should predominate. Soy legumes, such as edamame, tempeh, or tofu, are an excellent source of plant-based protein. The phytonutrients, protein, and healthy fats in soy all contribute to its anti-inflammatory properties. In fact, soy has been shown to decrease the inflammatory markers interleukin 6, TNF-α, and CRP.[58,59] At the same time, intake of non–soy-based legumes has been shown to have an inverse relation to high-sensitivity CRP.[60] Phytoestrogens in soy, daidzein and genistein, contribute to soy's reduction in systemic inflammation.[61] Finally, mushrooms are a good source protein, containing polyphenols and other anti-inflammatory phytonutrients.[62,63] It is recommended that mushrooms are cooked, to reduce natural carcinogens, as well as to release more nutrients, as they have a very tough cellular structure that is softened with cooking.[64]

## *Carbohydrates*

Although vegetables and fruits constitute the major source of carbohydrates in an anti-inflammatory diet, other carbohydrate types are incorporated. As in the Mediterranean and Okinawan

**Table 2.** Comparison of Sources of ω-6 and ω-3 Fatty Acids.[a]

| Food | Serving Size | Calories | ω-6 Linoleic Acid, g | ω-3, g | | |
|---|---|---|---|---|---|---|
| | | | | ALA | EPA | DHA |
| Salmon, sockeye, cooked, dry heat | 3 oz | 133 | 0.16 | 0.05 | 0.25 | 0.48 |
| Tuna in water, canned | 3 oz | 109 | 0.05 | 0.06 | 0.20 | 0.54 |
| Egg, poached | 1 large | 72 | 0.78 | 0.02 | 0 | 0.03 |
| Walnut, dry roasted | 1 oz | 180 | 9.93 | 2.38 | 0 | 0 |
| Flax seed, ground | 1 tbsp | 37 | 0.41 | 1.6 | 0 | 0 |
| Chia seed, dried | 1 oz | 138 | 1.7 | 5.1 | 0 | 0 |
| Sesame oil | 1 tbsp | 120 | 5.6 | 0.04 | 0 | 0 |
| Olive oil | 1 tbsp | 119 | 1.3 | 0.1 | 0 | 0 |
| Canola oil | 1 tbsp | 124 | 2.6 | 1.3 | 0 | 0 |

ALA, alpha-linolenic acid; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid.
[a]Data based on https://www.ars.usda.gov/northeast-area/beltsville-md/beltsville-human-nutrition-research-center/nutrient-data-laboratory/.

diets, whole grain carbohydrates with a low glycemic index are the mainstay for an anti-inflammatory diet. Consumers should choose their whole grains carefully, selecting grains with all their original parts present (bran, germ, and endosperm) and not the "refined" counterpart that strips out much of the nutrients. Moreover, grains that have been processed via the cracking or crushing should be limited due to their high glycemic index. Examples of whole grains include buckwheat, barley, rye, and wild rice. Most of these whole grains are also high in fiber, which has been shown independently to reduce inflammatory markers.[65-67]

### *Healthy Fats*

One of the significant differences between an anti-inflammatory diet and other diets is the emphasis on so-called anti-inflammatory fats. These fats may be present within foods classically categorized as fruits, vegetables, or protein, but they may also be added to the diet through supplementation of ω-3 FAs. Cold-water fish is one of the protein sources with the highest levels of ω-3 FAs, particularly salmon, sardines, and anchovies. The ω-3 FAs in these fish are especially beneficial, as they come preformed in eicosapentaenoic acid and docosahexaenoic acid, negating the need for conversion within the body. As fish oil has been shown to be a potent inhibitor of inflammation at doses higher than what can typically be acquired in food, it can be added as a supplement to an anti-inflammatory diet. A common recommendation is 1000 mg of fish oil, 3 times per day.[68]

Some eggs are also fortified with docosahexaenoic acid, but controversy remains regarding the impact of eggs on chronic disease.[69,70] With regard to plant sources of fats, flax seeds are rich in alpha-linolenic acid, which is less anti-inflammatory than eicosapentaenoic acid and docosahexaenoic acid but is a good source of ω-3 FAs. Other plant sources of alpha-linolenic acid include chia seeds, walnuts, and hemp seeds (see Table 2). In addition to maximizing ω-3 fat intake, trans FAs, which are proinflammatory, should be avoided.[9,71] When oils or fats are used to prepare foods, olive oil (mostly a monounsaturated fat) is the best choice when used at low temperatures.[72] Other oils that should be avoided—as they are proinflammatory—include soybean, cottonseed, peanut, and corn oil.[73]

## Additional Components

### *Tea and Alcohol*

In addition to the macronutrients that are included in an anti-inflammatory diet, other beverages can enhance anti-inflammatory processes. Drinking tea instead of coffee or sugary beverages can add an anti-inflammatory benefit. Tea is made by infusing the dried leaves of the plant *Camellia sinensis* in near boiling water, which releases antioxidants and polyphenols that contribute to reducing systemic inflammation. Green, black, and white teas contain these beneficial phytonutrients, with green and white having the highest levels.[74,75] As with other foods, sourcing tea that is organically produced will reduce any unintended proinflammatory impact from toxins or pesticides.

Moderate intake of alcohol, up to 1 drink per day for women and 2 drinks per day for men, is a component of both the Mediterranean and Okinawan diets.[76] Large studies have shown the cardiovascular benefit of moderate intake of alcohol as well as a reduction in inflammatory markers.[77,78] Heavy drinking, in comparison, showed higher levels of markers such as CRP.[79] Additionally, individual components of alcohol, such as resveratrol in red wine, have anti-inflammatory benefits.[80] However, the importance of moderation should be highlighted given the detrimental impact of heavy drinking on health and well-being, including increased cardiovascular disease and rates of certain cancers.[81,82] Ultimately, the recommendation for moderate intake should be made on an individual basis.

### *Spices and Herbs*

Many herbs and spices have an impact on inflammation similar to the other components of an anti-inflammatory diet and can enhance the overall anti-inflammatory effect when added. However, given that the doses of spices and herbs studied are quite high, including them as often as possible in an anti-inflammatory diet will increase the likelihood of impact on inflammation. Ginger and turmeric are the 2 herbs with the largest amount of data supporting their impact on inflammation. They inhibit IL-2, TNF-α, and IL-8, which are proinflammatory cytokines; they also inhibit leukotriene and prostaglandin synthesis.[83-87] Additionally, garlic, cayenne, and oregano have anti-inflammatory properties and should be added to food while preparing meals.[88]

### *Eating Patterns and Habits*

Beyond the dietary pattern of food selection, the manner in which food is consumed influences inflammation and nutrient value. Reinforced by complex social behaviors of Western society, Americans eat too much, too quickly, and on the run. Eating slowly, mindfully, and in smaller amounts can decrease the impact of inflammation on the body. Portion control and smaller meals decrease hyperglycemia and, in the long run, obesity—both of which reduce systemic inflammation.[89] Cortisol is a marker of stress in the body, and eating slowly, with a mindful approach, has been shown to decrease morning cortisol levels.[90] Changing the manner in which food is consumed may be equally as important as the food itself.

## Conclusion

Influenced by the Mediterranean and Okinawan dietary patterns, an anti-inflammatory diet has emerged from a growing knowledge about the proinflammatory and anti-inflammatory effects of food. Although the components of an anti-inflammatory diet have been evaluated individually, adherence to the overall dietary plan may yield the greatest benefit, as shown in studies of the Mediterranean diet.[91] As such, an anti-inflammatory diet should not be prescribed according to its isolated components. Moreover, a truly integrative anti-inflammatory approach to nutrition will focus on eating mindfully and in caloric balance to help decrease obesity. The definition of an anti-inflammatory diet will likely continue to evolve with further advancements in nutrition research.

### Statement of Authorship

Both authors contributed to the conception/design of the review; contributed to the acquisition, analysis, or interpretation of the data; drafted the manuscript; critically revised the manuscript; agree to be fully accountable for ensuring the integrity and accuracy of the work; and read and approved the final manuscript.

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