# *The effect of dairy products on* inflammatory biomarkers

**Inflammation is a biological process that occurs when the body activates an immune response to protect itself from environmental stimuli such as dietary triggers, pathogens or toxins.[1,2] Active inflammation, which typically involves redness, swelling or pain, is generally short lived. In contrast, chronic inflammation is a more persistent inflammatory response, which can trigger disease and illness.**

**There has been growing interest in evidence-based research on how the nutritional composition of dairy, such as its lipid profile, relative leucine content or fermentation status, can affect its inflammatory potential. This review reports the most recent research, which suggests that the consumption of milk and dairy protein has a neutral or beneficial effect on inflammatory biomarkers.**

## Types of inflammation

Acute inflammation is characterised by an acute-phase response that involves the activation of a cascade of various cytokines and inflammatory cells such as neutrophils, macrophages and monocytes. The acute-phase response manifests through fever, leukocytosis, increased synthesis of adrenocorticotropic hormones and the production of various acute-phase proteins (e.g. C-reactive protein, CRP). This response occurs in order to protect the host or repair tissue damage.

In chronic inflammation, activation of mononuclear cells such as lymphocytes, macrophages and plasma cells and an over-production of cytokines lead to tissue destruction, necrosis and illness owing to the immune system becoming unresponsive to substances or tissues that would normally induce an immune response.[3] Chronic inflammation is a key feature in obesity, atherosclerosis, cardiovascular disease, cancer, type 2 diabetes, and even neurodegenerative diseases.[4,5]

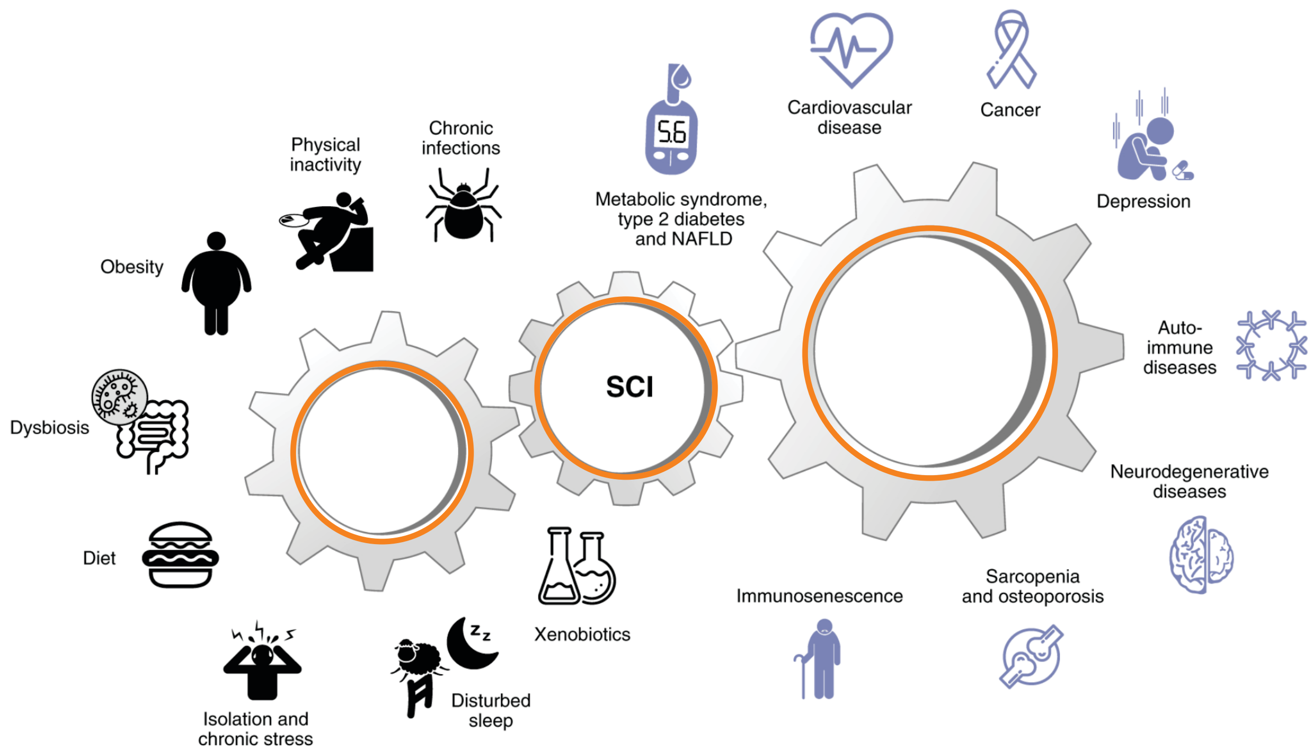


Figure 1:
Causes and consequences of low-grade systemic chronic inflammation (SCI) (Furman, 2019)[4]

## Causes of inflammation

**Inflammatory stimuli can include both endogenous and exogenous triggers:**

- Endogenous causes include DNA damage, dysfunctional telomeres (distinctive structures found at the ends of chromosomes), epigenomic disruption (epigenomes systematically control gene expression during development), disrupted mitogenic signals (mitogens are small proteins or peptides that induce cell division), and oxidative stress.
- Exogenous triggers include chronic infections, obesity, microbiome dysbiosis, diet, social and cultural changes, and environmental and industrial toxins.

Over time, a dietary pattern characterised by high consumption of proteins (from fatty domesticated and processed meats), saturated fats, refined grains, sugar, alcohol, salt and corn-derived fructose syrup, and a low intake of fruits and vegetables (as seen in typical Westernised diets),[6] can lead to post-prandial hyperlipaemia and hyperglycaemia. Spikes in the levels of triglycerides and glucose can also generate excess plasma reactive oxygen species that initiate pro-inflammatory reactions.[7] The inflammatory process therefore seems to be potentially modulated by dietary intake.[1]

## How does dairy impact inflammation?

**Dairy products, which include liquid milk, fermented products (such as yoghurt, kefir, maas, buttermilk and doogh), cheese, cream and butter, vary with regard to their food matrix and nutrient content.**

As a result, the effects of different dairy products on fat absorption, gut microbiota, gene expression and blood metabolomics vary, influencing lipid metabolism and inflammation.[2,8] In light of this, it is essential to consider the type of dairy before making dietary recommendations associated with inflammation.

## Effect of dairy on inflammatory markers

- In a randomised controlled trial to assess the effect of the consumption of low-fat dairy on systemic inflammation in patients with metabolic syndrome, Dugan et al.[9] found that female participants expressed significantly lower levels of tumour necrosis factor (TNF-α) and monochemo attractant protein-1 (MCP-1) after six weeks of consuming low-fat dairy compared with the control group who consumed no dairy. In addition, consumption of low-fat dairy significantly lowered the hepatic steatosis index (a screening tool for non-alcoholic fatty-liver disease)
- Van Meijl and Mensink[10] previously reported that overweight and obese research participants who consumed 500 ml low-fat milk and 150 g low-fat yoghurt daily demonstrated small decreases in TNF-α concentrations compared with participants who consumed carbo hydrate-rich control products (600 ml fruit juice and three fruit biscuits). However, there were no significant effects on markers of endothelial function and inflammatory response, such as serum MCP-1, IL-6, CRP, complement 3 and complement 4 (acute-phase proteins of the immune system) and either vascular or intracellular adhesion molecules.
- A systematic review by Zhang et al.[11] showed that a higher milk intake was related to a reduced risk of type 2 diabetes, metabolic syndrome and obesity. A dose–response analysis suggested that a 193 ml increment of milk intake per day was related to a 13% lower risk of metabolic syndrome and a 16% lower risk of obesity. Obesity is characterised as a chronic, low-grade, systemic inflammatory state that predisposes the body to developing other chronic conditions such as metabolic syndrome or type 2 diabetes.


## The effect of fermented dairy

- Burton et al.[12] reviewed a post-prandial response in healthy adults consuming yoghurt or acidified milk and found no significant difference in inflammatory biomarkers, including high-sensitive CRP, chemokines (MCP-1, MCP-1/CCL-2), IL-6, lipopolysaccharide and TNF-α. Both yoghurt and acidified milk intake appeared to regulate inflammatory genes; in particular, a significant down regulation of the expression of inflammatory genes was reported after two hours in participants who drank milk and after four hours in the group who consumed yoghurt.
- Rundblad et al.[8] demonstrated that a high-fat meal composed of fermented dairy products, and specifically cheese, had a lesser pro-inflammatory effect than intake of non-fermented high-fat dairy products, including butter and whipped cream. The high protein and calcium content of cheese may explain some of these differences. Only the non-fermented high-fat dairy products (i.e. butter and whipped cream) increased circulating concentrations of adhesion molecules.
- Pei et al.[13] found that in premenopausal women, daily consumption of 339 g low-fat yoghurt over nine weeks resulted in reduced concentrations of inflammatory biomarkers compared with intake of a non-dairy control food (soy pudding).
- The review of clinical trials by Bordoni et al.[1] concluded that fermented dairy products tend to have anti-inflammatory properties and that these effects are enhanced in participants with metabolic abnormalities.

## Dairy lipids

- Labonté et al.[14] concluded from the results of a randomised controlled trial among 112 participants with chronic low-grade inflammation that dairy consumption had no significant adverse effects on inflammatory markers in overweight or obese adults, despite the high saturated fat content of dairy foods.
- Similarly, a meta-analysis of cohort studies[15] revealed no significant relationship between dairy consumption and the risk of cardiovascular disease, despite the high saturated-fat content. It was suggested that milk intake might even be associated with an overall reduced risk of cardiovascular disease.
- Rundblad et al.[8] showed that high-fat meals that included butter, cheese, whipped cream or sour cream all induced a post-prandial inflammatory response. However, meals containing cheese or sour cream (fermented dairy products) induced a lesser pro-inflammatory response than those containing butter and whipped cream, despite having the same amount of fat and the same fatty acid composition. The response after cheese intake differed the most from that of the non-fermented products. Cheese contains more protein than the other three products, and plasma concentrations of amino acids were shown to have increased after intake of cheese compared with consumption of the other products. Cheese is also rich in calcium, which has been shown to suppress the inflammatory response by contributing to an anti-inflammatory gene expression response of peripheral blood mononuclear cells.[9]
- Moosavian et al.[16] reviewed 11 randomised controlled trials, which included 663 adult participants in total, and found that, compared with low or no dairy intake, high consumption of dairy products resulted in a decrease in CRP, TNF-α, IL-6, and MCP concentrations and increased adiponectin levels. These findings support the possible anti-inflammatory properties associated with dairy products. However, it must be kept in mind that between-study heterogeneity was considerable for CRP, TNF-α, IL-6, MCP and adiponectin, and moderate for leptin. Subgroup analysis showed that dairy consumption appeared to have no effect on inflammatory biomarkers and no differences were observed in these trials. The authors concluded that over the long term it appears that dairy products high in saturated fat do not promote inflammation because none of the studies reported an increase in circulating inflammatory markers in participants who received dairy.
- Similarly, the review by Ulven et al.[2] indicated that no pro-inflammatory effect was elicited in response to milk or dairy intake in healthy adults or those who were overweight, obese or had been diagnosed with metabolic syndrome or type 2 diabetes. Over the long term, it appears that dairy supplementation may, in fact, produce a weak anti-inflammatory effect in both population groups.

## Leucine

The high concentration of leucine in dairy may contribute to its anti-inflammatory properties,[16] possibly through increasing secretion of anti-inflammatory adiponectin and decreasing secretion of pro-inflammatory cytokines. In addition, leucine reduces oxidative and inflammatory stress by stimulating mitochondrial biogenesis, increasing oxygen consumption and fatty acid oxidation in adipocytes and skeletal muscle cells, and by inducing protein synthesis and suppression of protein degradation. Leucine can also increase sirtuin 1 secretion, which increases mitochondrial biogenesis and oxidative capacity. In turn, this prevents oxidative and inflammatory stress. SIRT1 inhibits the inflammatory nuclear factor kappa B pathway.

## Conclusion

**A large body of evidence shows that, in addition to dairy containing many nutrients important for growth and development, it does not appear to contribute to chronic inflammation and that fermented dairy products may, in fact, have anti-inflammatory properties. More evidence is needed to identify specific dairy foods as having anti-inflammatory potential.**

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