

Review Article**Dietary Strategies for Alleviating Inflammation and Metabolic Disorder:
A Narrative Review****Budhi Setiawan^{1*}, Ernawati¹**¹ Department of pharmacology, Medical Faculty Universitas Wijaya Kusuma Surabaya* Correspondence: budhisetiawan@uwks.ac.id**ABSTRACT**

Introduction: Inflammation plays a pivotal role in the pathogenesis of various health conditions, ranging from chronic diseases to autoimmune disorders. This narrative review delves into the intricate relationship between nutrition and inflammation, exploring the potential of dietary interventions as an alternative in mitigating metabolic conditions. **Method:** The relevant articles from databases such as PubMed, Scopus, Web of Science, and Google Scholar in the recent years have been extracted using the main keywords were: metabolic, omega 3, inflammation, gut microbiota, dietary pattern, polyphenols, dietary fiber, probiotics, and anti-inflammatory diet. **Result:** This review discussed the molecular mechanisms underlying inflammation and how certain dietary components can either exacerbate or mitigate these processes. The role of dietary patterns, such as the mediterranean, dietary approach to stop hypertension (DASH), plant-based diet, and anti-inflammatory diets, in promoting overall health and reducing inflammation. These patterns emphasize the consumption of whole foods rich in anti-inflammatory agents while minimizing pro-inflammatory substances. The complex interaction between the gut microbiota and dietary factors, underscoring the bidirectional relationship that influences inflammatory outcomes. **Conclusion:** the multifaceted exploration presented herein underscores the potential of nutrition as a modifiable factor in promoting anti-inflammatory environments within the body.

Keywords: Inflammation, dietary pattern, metabolic disease, anti-inflammatory diet.**Strategi Diet untuk Mengurangi Inflamasi dan Penyakit Metabolisme:
Sebuah Tinjauan Pustaka Naratif****ABSTRAK**

Pendahuluan: Inflamasi memainkan peranan penting dalam patogenesis berbagai masalah kesehatan, mulai dari penyakit kronis hingga gangguan autoimun. Tinjauan pustaka naratif ini menggali hubungan yang kompleks antara nutrisi dan inflamasi serta mengeksplorasi potensi intervensi diet sebagai alternatif dalam mencegah penyakit metabolisme. **Metode:** Artikel-artikel yang relevan dari pangkalan data ilmiah seperti *PubMed*, *Scopus*, *Web of Science*, dan *Google Scholar* yang dipublikasikan dalam beberapa tahun terakhir. Ekstraksi data menggunakan beberapa kata kunci seperti misalnya metabolik, omega 3, inflamasi, mikrobiota usus, pola diet, polifenol, makanan berserat, dan diet anti inflamasi. **Hasil:** Tinjauan ini membahas mekanisme molekuler yang mendasari inflamasi dan bagaimana komponen-komponen di dalam makanan dapat memperburuk atau meringankan proses-proses tersebut. Peran pola diet, seperti diet mediterania, *dietary approach to stop hypertension* (DASH), pola diet makanan nabati, dan diet anti-inflamasi dalam upaya meningkatkan kesehatan serta mengurangi inflamasi. Pola-pola diet tersebut menekankan konsumsi makanan seutuhnya yang kaya akan zat-zat anti-inflamasi dengan meminimalisir kandungan zat-zat pro-inflamasi. Interaksi yang kompleks antara mikrobiota usus dan faktor diet makanan, menunjukkan pentingnya hubungan dua arah yang dapat mempengaruhi akibat dari inflamasi. **Kesimpulan:** Eksplorasi multifaset yang disajikan di tinjauan ini menggarisbawahi potensi nutrisi sebagai faktor yang dapat dimodifikasi dalam meningkatkan kondisi anti-inflamasi di dalam tubuh.

Kata kunci: Inflamasi, pola diet, penyakit metabolik, diet anti-inflamasi.

INTRODUCTION

As a significant component in the pathogenesis of many diseases, including metabolic diseases, chronic inflammation has been identified (Bennett et al., 2018; Furman et al., 2019). Disorders like metabolic diseases, cardiovascular diseases, and respiratory diseases have been linked to the start, development, and aggravation of dysregulated inflammatory processes (R. Wang et al., 2021). Beyond its role in specific disease etiologies, chronic inflammation is increasingly recognized as a common thread underlying aging and age-related diseases (Furman et al., 2019).

The molecular mechanisms driving inflammation involve a complex interplay of cytokines, immune cells, and signaling pathways. Persistent activation of these pathways can lead to tissue damage, contributing to the perpetuation of pathological conditions (L. Chen et al., 2018). As a consequence, mitigating chronic inflammation has become a crucial focus for therapeutic interventions and preventive strategies.

The intimate link between diet and inflammation provides a compelling rationale for delving into nutritional strategies as a means of alleviating inflammatory conditions. Epidemiological and clinical studies have consistently demonstrated the influence of dietary patterns on the modulation of inflammatory biomarkers (Santos, 2022). For instance, diets rich in omega-3 fatty acids, antioxidants, and polyphenols have shown promising anti-inflammatory effects in various populations (Siroma et al., 2021).

The potential of nutrition to impact inflammatory responses is not only supported by empirical evidence but also grounded in the molecular understanding of how specific nutrients can regulate immune function and inflammatory pathways (Munteanu & Schwartz, 2022; Tourkochristou et al., 2021). Consequently, exploring nutritional strategies offers a

promising avenue for interventions that are both accessible and sustainable.

This outline provided a structured framework for organizing the information in this narrative review, therefore the aim of this work was to give a comprehensive and coherent exploration of nutritional strategies for alleviating inflammatory conditions.

METHOD

A search was conducted using date limits in the electronic databases such as PubMed, Web of Science, Scopus, and Google Scholar up to December 2023, no date restrictions were used. Search phrases for microbiota ("Microbiota," "Dysbiosis," "Gastrointestinal microbiome"), food ("Diet," "Dietary pattern," "Nutrition," "Fiber"), and chronic inflammatory disorders ("Metabolic diseases," "Inflammation," "Diabetes Mellitus," "Cardiovascular disease") were combined. Duplicate articles were removed, and only items written in English were included.

INFLAMMATORY DISEASES

A growing amount of research now indicates that many age-associated chronic diseases are due to low-grade, persistent inflammation that is unrelated to acute causes (Tracy, 2003). In particular, inflammation of the endothelium has been linked to conditions such as cardiovascular disease (CVD) and hypertension. Furthermore, it has been linked to the development of insulin resistance, type 2 diabetes (T2D), and about 15% of malignancies, including thyroid, esophageal, bladder, and prostate cancers. (Balkwill & Mantovani, 2001; Mantovani et al., 2008; X. Wang et al., 2013). Additionally, there is evidence to suggest that neuroinflammation may have a role in the development of dementia, depression, and cognitive decline. (Miller & Spencer, 2014). These ailments represent significant risk factors for

morbidity and mortality during the aging process (Franceschi et al., 2000). Serum inflammatory indicators can be measured to assess inflammation, even low-grade forms. While lower levels of adiponectin signify reduced inflammation, elevated levels of C-reactive protein (CRP), interleukin 6 (IL-6), tumor necrosis factor α (TNF- α), and fibrinogen indicate heightened systemic inflammation (Brenner et al., 2014; Davalos & Akassoglou, 2012; Fantuzzi, 2008).

DIETARY PATTERNS

There are several effective dietary patterns for reducing the risk of chronic diseases. Here are some ideas based on the search results:

Mediterranean diet: It is a conventional eating plan that prioritizes whole grains, seafood, fruits, vegetables, and healthy fats like nuts and olive oil. The Mediterranean diet is useful in lowering the risk of cardiovascular illnesses and total mortality, according to research that has repeatedly demonstrated this (Laffond et al., 2023; Martínez-González et al., 2019). A decreased risk of chronic illnesses like obesity, hypertension, diabetes mellitus, and cognitive decline has also been linked to a Mediterranean diet (Aridi et al., 2020).

DASH diet: A dietary pattern known as the Dietary Approaches to Stop Hypertension (DASH) diet places an emphasis on fruits, vegetables, whole grains, fish, chicken, legumes, and nuts in addition to low-fat dairy products (Suri et al., 2020). The DASH diet is a healthful eating pattern that has been shown to lower blood pressure and lower the risk of cardiovascular disease (Filippou et al., 2020). In addition, the DASH diet has been demonstrated to help reduce insulin resistance, triglycerides, low-density lipoprotein (LDL)-C, and blood glucose levels, making it a crucial supplement to pharmaceutical therapy for metabolic disorders (Campbell, 2017).

Plant-based diet: The dietary pattern limits or stays away from animal products in favor of plant foods such fruits, vegetables, whole grains, legumes, nuts, and seeds.

Following a plant-based diet has been linked to a decreased risk of cancer, death, and especially cardiovascular disease (Thompson et al., 2023). Adults who consume a nutritious plant-based diet low in animal products, sugar-filled beverages, snacks, sweets, refined grains, potatoes, and fruit juices are at a lower risk of developing serious chronic illnesses and dying young (Thompson et al., 2023).

Anti-inflammatory diet: it aims to reduce inflammation in the body and has been linked to a decreased risk of chronic conditions such as cardiovascular disease, autoimmune diseases, and neurological diseases (Stromsnes et al., 2021). An anti-inflammatory diet aims to replace pro-inflammatory foods with anti-inflammatory ones in order to help lower the body's inflammatory indicators (Li et al., 2020). Some key aspects of an anti-inflammatory diet include: Fruits and vegetables, whole grains, omega-3 fatty acids, dairy products, herbs and spices, and probiotics. However, it is essential to note that there is no well-defined anti-inflammatory diet, and individual dietary needs and preferences may vary.

MICROBIOTA AND INFLAMMATION

Diets anti-inflammatory can have a major effect on gut flora, according to studies. Dietary variables can modify the gut microbiota, which in turn affects the body's balance of pro- and anti-inflammatory responses. Studies have demonstrated that diets rich in fish, vegetables, legumes, grains, nuts, and plant-based foods, together with a greater consumption of plant-based foods relative to animal-based foods, can support the development of an anti-inflammatory gut ecosystem (Bolte et al., 2021). Furthermore, a diet high in plant-based foods-legumes, veggies, fruits, nuts, and low-fat fermented dairy and fish-has been linked to the possibility of preventing inflammatory processes in the intestines through the action of the gut microbiota. Furthermore, through influencing the gut microbiota and regulating inflammatory

responses, anti-inflammatory substances, foods, and diets have been shown to be crucial in the management of obesity (Bagheri et al., 2022). Particularly, it has been demonstrated that consuming unprocessed and minimally processed foods, fiber, mono- and polyunsaturated fatty acids, lean protein sources, and different spices, along with consuming less red meat, high-fat dairy products, and saturated and trans fats, will alter the gut microbiota and reduce inflammation (Bagheri et al., 2022).

Inflammation represents the body's innate defence mechanism triggered automatically in response to the invasion of foreign pathogens. However, a number of illnesses, including as cancer, obesity, cardiovascular disease, and neurological disorders are associated with an overabundance of inflammation. Numerous studies have demonstrated a direct correlation between dysbiosis, or changes in gut microbiota, and inflammatory diseases like obesity and inflammatory bowel disease. (J. Wang et al., 2020), immune-mediated inflammatory diseases like ulcerative colitis, Crohn's disease, rheumatoid arthritis, and multiple sclerosis (Forbes et al., 2018), as well as type I and II diabetes mellitus (Meijnikman et al., 2018). The relationship between inflammation and gut microbiota is impacted by important host-related variables, including antibiotic use, body mass index (BMI), age, gender, and dietary habits. As previously reviewed, dysbiosis is recognized as a critical factor in both chronic inflammatory and metabolic dysfunction (Khan et al., 2019). Notably, through a variety of pathways, short-chain fatty acids (SCFAs), in particular acetate, propionate, and butyrate, produced by microbial fermentation of undigested food, are essential for preserving colonic health. According to van der Beek's 2017 description, short-chain fatty acids (SCFAs)' anti-inflammatory and anticarcinogenic properties help colonocytes maintain metabolic homeostasis (van der Beek et al., 2017). Alsharairi (2021), in a non-systematic review, extensively discussed the

therapeutic potential of SCFAs derived from infant intestinal microbiota in addressing obesity (Alsharairi, 2021). Numerous investigations have demonstrated that short-chain fatty acids (SCFAs) had a role in inflammation (Yao et al., 2022) and exerted a regulatory influence on macrophages (Berthold et al., 2021; Huang et al., 2022), epithelial cells (Pérez-Reytor et al., 2021), neutrophils (Kim, 2021), and monocytes (Pujari & Banerjee, 2021).

HIGH FIBER DIET

Dietary fiber consists of plant-derived soluble and insoluble carbohydrates that resist digestion by human enzymes, remain unabsorbed in the small intestine, and positively impact human health (Waddell & Orfila, 2023). Numerous studies have explored the correlation between dietary fiber and obesity, revealing a significant reduction in obesity associated with increased fiber consumption (J.-P. Chen et al., 2017; Jovanovski et al., 2021; Waddell & Orfila, 2023). Additionally, research has established that dietary fiber intake influences the composition and activity of gut microbiota (Chambers et al., 2019; David et al., 2014). The association between a lower incidence of Type 2 diabetes and a higher consumption of dietary fiber has been confirmed by both epidemiological and randomized controlled studies. (Reynolds et al., 2019).

Research indicates that increased colonic production of SCFAs, such as acetate, propionate, and butyrate, which are byproducts of gut microbiota-mediated fermentation of dietary fiber, is responsible for the positive effects of dietary fiber on improving insulin sensitivity (Flint et al., 2012; Macfarlane & Macfarlane, 2003). In fact, studies using animal models have shown that a high-fiber diet can lead to elevated levels of circulating SCFAs, which have anti-inflammatory properties. In a human investigation, participants on a high-fiber diet showed significantly higher levels of acetate and propionate when compared to those on a low-fiber diet. However,

throughout the brief five-day intervention period, there were no changes in peripheral blood inflammatory markers (Gill et al., 2020).

When gut microbiota and SCFAs were analyzed in American and Ghanaian women, the latter of whom consumed significantly more dietary fiber, it was found that the lean Ghanaians had more microbial genes that were involved in catalyzing the production of butyric acid by fermentation of pyruvate or branched-chain amino acids. On the other hand, independent of BMI, obese Ghanaian and American women showed a greater frequency of microbial genes linked to enzymes involved in the fermentation of amino acids, including alanine, aspartate, lysine, and glutamate (Dugas et al., 2018).

POLYPHENOLS

Plant secondary metabolites known as polyphenols are among the most common antioxidants present in foods we eat on a regular basis. Due to their complex chemical makeup and large molecular weight, the gastrointestinal tract absorbs very little of the dietary polyphenols. But the intestinal bacteria in the large intestine changes them into smaller molecular weight bioactive phenolic compounds (X. Wang et al., 2022). Several clinical research investigating the relationship between intestinal microbiota and obesity have revealed the beneficial effects of polyphenols in modifying gut microbiota to reduce obesity (Ma & Chen, 2020). Significantly, a carefully monitored clinical study showed that eating oranges on a regular basis improved the makeup and activity of the gut bacteria. This resulted in increased synthesis of short-chain fatty acids (SCFAs) and an increase in *Bifidobacterium* and *Lactobacillus* species. Moreover, it enhanced metabolic indicators like insulin sensitivity, glucose levels, and low-density lipoprotein (LDL) cholesterol (Lima et al., 2019). In another randomized controlled trial (RCT), it was shown that giving obese people a two-month supply of the flavonoid genistein reduced their insulin resistance, decreased their metabolic endotoxemia,

phosphorylated more 5'-adenosine monophosphate-activated protein kinase, and increased their skeletal muscle fatty acid oxidation (via changes in gene expression). Changes in the gut microbiota, namely a rise in the *Verrucomicrobia* phylum, were blamed for these consequences (Guevara-Cruz et al., 2020). Results from a randomized controlled trial (RCT) with individuals at high cardiometabolic risk confirmed that diets high in polyphenols increased the diversity of dominating fecal bacteria and that these changes were connected with modifications in glucose/lipid metabolism (Vetrani et al., 2020a).

OMEGA 3 RICH DIET

Fatty acids with 18 or more carbon atoms are known as long-chain polyunsaturated fatty acids (LC). They are divided into two main families, $\omega 3$ (LCn3) and $\omega 6$ (LCn6), according to where the fatty acid's initial double bond is located in relation to its methyl end group. (Abedi & Sahari, 2014). Results from a randomized controlled study (RCT) with participants at high cardiometabolic risk showed that LCn3-rich meals affected the composition of the gut microbiota in these participants. Following both low-LCn3 and polyphenol-rich and high-LCn3 diets, it was shown that the diversity of dominating fecal bacteria reduced; these changes were associated with modifications in glucose/lipid metabolism (Vetrani et al., 2020b). An additional trial with 126 patients who had borderline hypercholesterolemia showed a significant rise in the relative abundance of a particular species, *Clostridium leptum*, following a dietary intervention. At the same time, a number of metabolic health-related plasma markers showed notable improvements, including triglyceride levels, total cholesterol to HDL ratio, and apolipoprotein B. The generation of butyrate was also covered in this study as a possible method for improving the blood lipid profile (Lim et al., 2022).

PROBIOTICS

Non-pathogenic microorganisms that enter

the gut in an active state and may benefit the host are referred to as probiotics (Ohland & MacNaughton, 2010). Probiotics have been shown in numerous studies to have beneficial impacts on parameters linked to inflammation and obesity in addition to having an impact on the gut microbiota (Hibberd et al., 2019; Stenman et al., 2016). Serum levels of IL-1 β , TNF- α , and CRP were significantly reduced in an intervention involving *Bifidobacterium* and *Lactobacillus* (probiotic yogurt), but serum levels of IL-6 and IL-10 were noticeably increased. (Shadnough et al., 2013).

A low-energy diet alone causes changes in metabolite profiles linked to decreased inflammation and positive effects on body weight, according to a double-blind randomized controlled trial (RCT) conducted on obese women. The results showed that metabolites linked to better metabolic health are altered by probiotics and synbiotics alike. Significantly, the results showed that synbiotics may be more beneficial than probiotics or diet alone if they are combined with particular metabolite modifications and a low-energy diet (Crovesy et al., 2021). A 2021 meta-analysis of RCTs revealed that a synbiotic, which is characterized as a mix of live microorganisms and selectively employed substrate(s) favorable to host health, significantly lowers levels of LDL-cholesterol, triglycerides, and total cholesterol (C. Wang et al., 2021). An RCT conducted in 2022 found that supplementing with the probiotics under study improved the function of the intestinal barrier and led to a significant decrease in the amounts of lipopolysaccharides (LPS). Additionally, it significantly raised levels of SCFAs, specifically propionic and butyric acid, and enhanced indicators linked to obesity (Chaiyasut et al., 2022). Treatment with multispecies probiotics changed the gut microbiota's physiological, immunological, and biochemical parameters in obese postmenopausal women, but it had no effect on the taxonomic categorization or diversity

of the bacteria (Kaczmarczyk et al., 2022).

CONCLUSION

In general, following a healthy dietary pattern was associated with reduced levels of inflammation and metabolic diseases. Dietary habits that follow well-known healthy diets were more likely to be associated with decreased inflammation. Adopting a possible outcomes strategy in long-term longitudinal studies with repeated assessments of inflammation and diet was necessary to strengthen the evidence for a causal association between dietary patterns and inflammation.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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