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Review Article

The Role of Healthy Dietary Patterns in Managing Chronic Low-Grade Inflammation - A Literature Review

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Abstract

Introduction: Although the importance of healthy dietary patterns in preventing non-communicable diseases has been well researched, the picture regarding their role in managing chronic low-grade inflammation remains unclear. This review gives an overview of the mechanisms through which healthy dietary patterns affect chronic low-grade inflammation.

Methods: A critical appraisal of the current literature was conducted to identify the effects of the Mediterranean diet, DASH diet, and plant-based diet on chronic low-grade inflammation.

Results: Most studies revealed a significant positive effect of the three dietary patterns against chronic low-grade inflammation via various physiological routes. Their protective role was explained by the high amounts of vitamins, minerals, long chain unsaturated fatty acids, and fibers that possess antioxidant functions and prohibit several pro-inflammatory mediated mechanisms. Following healthy dietary patterns was also found to induce weight loss which has been previously shown to independently reduce chronic low-grade inflammation.

Conclusion: Following healthy dietary patterns should be recommended by health care practitioners and dietitians as a therapeutic lifestyle approach aimed at managing chronic low-grade inflammation, especially among individuals at high risk of non-communicable diseases. Future randomised controlled trials with robust methodologies are needed to determine the most effective dietary pattern for improving chronic low-grade inflammation.

Keywords: Diet, Dietary patterns, Inflammation, Chronic Low-Grade Inflammation, Inflammatory markers, Mediterranean diet, Dietary Approaches to Stop Hypertension, Plant-based diet, Non-communicable diseases.

Background

Chronic low-grade inflammation is a natural biological reaction where the human body persistently produces specific types of inflammatory chemicals in defensive response to harmful lifestyle conditions (e.g., obesity, visceral fat accumulation, smoking, unhealthy food intake, and/or physical inactivity) [1]. For instance, the excessive accumulation of adipose tissues in the body upregulates the pro-inflammatory genes, downregulates the anti-inflammatory genes, and produces adipokines (e.g., leptin, resistin) that contribute to chronic low-grade inflammation [2]. Even though its definition is not standardised, chronic low-grade inflammation has been directly linked with elevated levels of circulating chemical biomarkers that promote disease progression [3]. These include cytokines such as Interleukins (IL-6, IL-8, and IL-1 beta), Tumor Necrosis Factor-Alpha (TNFα), C-Reactive Protein (CRP), and adhesion molecules (e.g., Intracellular Adhesion Molecule 1 (ICAM-1) and Vascular Cell Adhesion Molecule 1 (VCAM-1)) [4].

Recent studies have linked chronic low-grade inflammation with non-communicable diseases such as type Two Diabetes Mellitus (T2DM), Cardiovascular Diseases (CVD), atherosclerosis, cancer, depression, and metabolic syndrome [5,6,7]. Physiologically, chron-

ic low-grade inflammation disrupts the body's homeostasis, modifies the interactions between immune and metabolic pathways, and eventually fosters chronic inflammatory mechanisms [6]. This phenomenon, referred to as "meta-inflammation", stimulates the infiltration of immune cells and the continual release of inflammatory cytokines into the surrounding tissues leading to modifications in glucose and lipid metabolisms [7]. The prolonged tissue exposure to the released inflammatory cytokines causes insulin resistance, which, if untreated, leads to T2DM [7]. Additionally, the persistent inflammatory status causes atheroprogression that significantly contributes to the development of cardiovascular diseases [8]. Chronic low-grade inflammation also facilitates the advancement of various types of cancer through inducing cell proliferation, reducing apoptosis, and promoting angiogenesis and metastasis [9].

Diet constitutes a major modifiable risk factor that plays a significant role in affecting chronic low-grade inflammation and consequently the risk of non-communicable diseases [10]. For example, recent studies have shown that unhealthy dietary patterns, such as the Western Diet, serve as a pro-inflammatory factor for it leads to altering the gut environment, impairing the immune system, and decreasing the synthesis of anti-inflammatory cytokines [10]. These unhealthy dietary patterns are characterised by low amounts of polyunsaturated fatty acids, whole grains, fruits, vegetables, and fibers and high amounts of refined carbohydrates, sweets, and saturated fats [11]. On the contrary, healthy dietary patterns, that are high in fruits, vegetables, and fibers and low in saturated- and trans-fats, have been found to support the immune system and reduce inflammation [12]. Furthermore, they have been shown to protect against obesity, hypertension, cardiovascular diseases, diabetes, and cancer [12]. Examples of healthy dietary patterns include the Mediterranean Diet (MD), Dietary Approaches to Stop Hypertension (DASH diet), and Plant-Based Diet (PBD).

Although the protective effect of healthy dietary patterns against non-communicable diseases has been well researched, their role in managing chronic low-grade inflammation remains unclear. This review aims to advance the knowledge about the relationship between healthy dietary patterns and chronic low-grade inflammation by critically appraising the literature around the effects of the Mediterranean, DASH, and plant-based dietary patterns on various inflammatory body mechanisms.

Mediterranean Diet and Chronic Low-Grade Inflammation

The Mediterranean Diet (MD) is one of the famous healthy dietary patterns characterised by high intake of fruits, vegetables, whole grains, olive oil, and nuts and low in sweets, red meat, and saturated fats [13]. It is also characterised by moderate consumption of wine, dairy products, and seafood [13]. Given that healthy dietary patterns offer protective benefits against numerous chronic diseases, recent studies have proposed that the Mediterranean Diet could potentially mitigate chronic inflammatory processes [14].

Evidence indicates that higher adherence to Mediterranean Diet enhances endothelial function and reduces the levels of circulating inflammatory markers [15]. For instance, a systematic review and meta-analysis of 17 randomised controlled trials, that assessed the relationship between MD and inflammation, reported that the high adherence to MD among the intervention group resulted in a significant decrease in inflammatory markers CRP and IL-6 compared to the control group who had low MD adherence [16]. Another meta-analysis of 6 randomised controlled trials also found that obese participants who followed the MD for two years had a significantly decreased levels of CRP and improvements in endothelial functions evident through measurements of Flow-Mediated Dilation (FMD), where the FMD % was double the baseline values [17]. However, the studies included in the analyses of those reviews had several limitations such as high heterogeneity due to methodological discrepancies and grouping studies that focused on inflammation alone as the main outcome with studies that focused on several diseases including inflammation. Interestingly, one study found no effect of the Mediterranean diet on inflammatory markers CRP and IL-6 [18]. In that study, female participants were divided into an intervention group where they followed MD for 4 weeks and a control group that followed a standard diet. The findings showed only significant increases in blood omega-3 fatty acid levels with no effect on CRP or IL-6 levels. However, since the study was conducted among women, it might be hard to generalise the results to the whole population. Given that men are at higher risk of CVD and chronic low-grade inflammation [19], including male participants in the study could have altered the significance of the findings. Moreover, the 4-week duration of the intervention might be insufficient for detecting any effect of MD on the inflammatory profile.

MD-induced Weight Loss and Chronic Low-Grade Inflammation

Intervention studies indicate that the reduction in body fat impairs the gene expression of inflammatory markers, resulting in lower mRNA levels of cytokines [20]. Furthermore, randomised controlled trials have found that weight loss significantly decreases the release of CRP, IL-6, IL-18, TNF-α from abdominal adipose tissues [21-24]. The adherence to Mediterranean diet is globally recommended as an integral part of obesity management for it has been proven to induce weight loss and improve body functions [25,26]. However, whether the enhancements in the inflammatory profile upon following the Mediterranean diet is due to the MD-induced weight loss or the diet itself is discussed below.

A randomised controlled trail (RCT) by *Esposito et al.* [27] assigned a low-calorie MD to a group of childbearing aged women against a control group. The authors observed a significant augmentation in Adiponectin (anti-inflammatory hormone) and a significant decrease in CRP and IL-6 among the intervention group. These improvements in the inflammatory status among the study's intervention group were assumed to be due to the weight loss effect and not directly caused by the MD. This issue has been addressed by the same authors in another study [28], where similarly results showed that participants with metabolic syndrome, who lost weight after following the MD for two years, had a significant improvement in the circulatory level of CRP, Il-6, and IL-18 compared to the control group. When the authors controlled for weight loss as

a confounding factor in the study's analysis, the anti-inflammatory effect of the MD remained significant among the intervention group proposing that it is induced by other mechanisms independent of weight loss.

Within this context, a review by *Calder et al.* [29] argued that the main anti-inflammatory effect of the MD is explained by its micronutrient content. For example, vitamins (specifically vitamins E and C) from fruits and vegetables, omega-3 fatty acids from seafood, and mono-unsaturated fatty acids from olive oil have been shown to alter the chemical composition of free radicals that lead to oxidative damage of body cells, inhibit the expression of inflammatory genes and the proinflammatory transcription factor (nuclear factor kappa B (NF-κB)), and activate the anti-inflammatory transcription factor (Peroxisome Proliferator Activated Receptor Gamma).

DASH Diet and Chronic Low-Grade Inflammation

The DASH diet is known to be high in fruits and vegetables, skimmed milk, whole grains, fish, and chicken and low in overall fats (trans, saturated, and cholesterol), red meats, and sugar [30]. It is also low in salt (sodium) and high in magnesium, calcium, potassium, and fiber [30]. Studies investigating the effect of DASH diet on chronic low-grade inflammation are few, but the majority highlight its protective role.

An RCT by *Asemi et al.* [31] reported no significant impact of the DASH diet on CRP levels in individuals with gestational diabetes (24 weeks). Additionally, *Taheri et al.* [32] found that the DASH diet did not significantly alter serum levels of Monocyte Chemoattractant Protein-1 (MCP-1), an inflammatory cytokine, when compared to other dietary patterns. In contrast, *Fung et al.* [33] demonstrated a significant association between the DASH diet and reduced levels of serum interleukin-6 (IL-6) and C-Reactive Protein (CRP). Similarly, previous studies [34-36] have indicated that the DASH diet positively influences serum CRP and high-sensitivity CRP (hs-CRP) levels. A crossover study by *Azadbakht et al.* [37] including 31 diabetic individuals also found that serum CRP was significantly decreased in the intervention group following a DASH diet (mean decline = -26,5%) compared to the control group (mean decline = -5%). Despite the results of the study, the sample size comprised a major limitation and a carry-over bias might have occurred where the effectiveness of the second treatment is influenced by the impact of the first treatment. These findings are consistent with those of another RCT conducted among 48 obese females who had polycystic ovary syndrome [38]. In that study, participants in the intervention group followed the DASH diet for 2 months and those in the control group followed a standard diet. The authors found that participants following the DASH diet had significantly lower CRP blood levels compared to the control group (-763.29 vs. 665.95 ng/m), in addition to reduced body weight and blood insulin levels.

The protective role of the DASH diet in managing chronic low-grade inflammation has several explanations. *King et al.* [39] argues that the high consumption of fiber in the DASH diet is key, where evidence indicates that consuming 30 grams per day of fibers was found to be associated with decreased CRP levels [40,41]. Moreover, the high content of fruits, vegetables, and flavonoids in the DASH diet, have been found to exhibit antioxidant properties leading to reduction in free radicals, lipid peroxidation, and chronic low-grade inflammation [42]. For instance, *Holt et al.* [43] found that a high intake of fruits and vegetables was linked to lower levels of IL-6, CRP, and TNF-α. Other studies have linked the protective effects of the DASH diet to the low salt (sodium) intake. For instance, a population-based study by *Fogarty et al.* [44] among 2,633 participants found that the elevated levels of CRP were significantly associated with high sodium intakes. Additionally, phytochemicals and the bioactive compounds found in the DASH diet are key modulator that have been shown to improve intestinal permeability, thereby reducing the body's vulnerability to infection, and consequently inflammation [12].

Plant-Based Diet and Chronic Low-Grade Inflammation

The Plant-Based Diet (PBD) primarily comprises foods derived from plants, with minimal or no inclusion of animal products (e.g., vegan/vegetarian diets) [45]. This dietary pattern is characterised by a high intake of fiber-rich plant foods, such as vegetables, fruits, whole grains, legumes, nuts, and seeds, while limiting the consumption of animal-derived foods [45]. Current evidence about the impact of PBD on inflammatory biomarkers remains limited, hindering definitive conclusions about its role in managing chronic low-grade inflammation [46].

To date, studies that comprehensively examined the relationship between the vegan diet and the inflammatory profile are scarce. For instance, only two studies have provided data on inflammatory biomarkers in small cohorts of vegans (n = 9) [47] or strict vegetarians (defined as consuming animal products less than once a month) (n = 66) [48]. Both studies focused primarily on advanced glycation end products or gut microbiota composition but showed different results. While *Franco-de-Moraes et al.* [48] reported elevated CRP levels in the cohort following a vegan diet, *Šebeková et al.* [47] found no significant effect.

The impact of the vegetarian dietary pattern on inflammatory biomarkers has been examined also in few studies [49, 50]. For example, a systematic review and meta-analysis by *Craddock et al.* [50] reported that only four from the seven studies, that assessed the association between a vegetarian diet and CRP levels, demonstrated significant negative correlations. The authors found that, aside from CRP, other inflammatory biomarkers have either not been reported or have been examined in a limited number of studies. This lack of comprehensive data restricts the ability to draw definitive conclusions regarding the impact of the vegetarian diet on the wider inflammatory profile [50]. Notably, *Haghighatdoost et al.* [49] indicated that individuals adhering to a vegetarian diet for a minimum of two years tend to exhibit lower CRP levels. In contrast, no significant effects were observed in participants who followed the diet for less than two years [49].

Consistent with these findings that highlighted the importance of the duration of adhering to the plant-based diet, *Menzel et al.* [51] also found that individuals who followed the vegan diet for more

than 4.8 years were found to have lower levels of hs-CRP compared to those who followed the diet for 4.8 years or less. Additionally, the increased blood concentrations of resistin, IL-1, and IL-18 were found to be strongly correlated with the duration of adherence to the vegan diet among study participants. Given this context, studies have proven that the elevated levels of resistin, hs-CRP, IL-1, and IL-18 are associated with the onset of insulin resistance and pro-inflammatory processes that lead to a range of serious metabolic, inflammatory, and autoimmune disorders [52,53].

Further research with robust design and methodology is required, not only to explore the relationships between vegan or vegetarian dietary patterns and inflammatory biomarkers, but also to investigate the impact of both short-term and long-term adherence to vegetarian or vegan diets on chronic low-grade inflammation. Such studies could add a valuable insight to the body of knowledge by determining potential benefits of these diets in preventing inflammatory conditions, thereby reducing the risk of chronic diseases.

Conclusion

This literature review provides an enthusiastic insight about the role of healthy dietary patterns such as the Mediterranean, DASH, and plant-based diets in managing chronic low-grade inflammation. Despite the heterogeneity in the studies' outcomes, evidence indicates that healthy dietary patterns reduce chronic low-grade inflammation via various physiological routes that restrain deleterious mechanisms and protect against non-communicable diseases [3,4,12].

The beneficial effects of the healthy dietary patterns have been explained by their high amounts of vitamins, minerals, phytochemicals, long chain unsaturated fatty acids, and fibers that possess antioxidant functions and prohibit several pro-inflammatory mediated mechanisms [18,27]. In addition, consuming healthy diets induces weight loss which also contributes to reducing chronic low-grade inflammation [29]. This is not to say that the anti-inflammatory role of healthy dietary patterns is solely dependent on weight loss. In fact, evidence has shown that their effect remains significant even after controlling for weight loss, which has been explained by the diets' nutritional contents [28]. Therefore, the scientific evidence discussed in this review may not be exclusive to the Mediterranean, DASH, and plant-based dietary patterns, but can also be applied to newly developed/updated healthy dietary patterns that constitute similar food and nutrient composition, regardless of the name or label.

Although the Mediterranean Diet seems to be the most protective among other healthy dietary patterns against chronic low-grade inflammation, future studies should examine the effects of all healthy dietary patterns among the same cohort to provide definitive evidence about the most beneficial one in managing chronic low-grade inflammation. At a clinical level, the evidence discussed in this review might be useful to implement nutritional strategies aimed at lowering inflammation and improving the health of the population. Dietitians and health care practitioners should also translate this evidence on the role of healthy dietary patterns to practical dietary advice, especially for individuals at high risk of non-communicable diseases and/or chronic low-grade inflammation.

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Conflicts of Interest

The authors declare no conflicts of interest.

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