

Effect of molecular hydrogen as a nutrient on the inflammatory index of diet, with reference to health promotion and disease prevention

Abstract

Western dietary patterns are associated with chronic low grade inflammation, which is risk factor of cardiovascular diseases (CVDs) and other non-communicable diseases (NCDs). Increased consumption of Mediterranean type of foods are anti-inflammatory, which may cause decrease in the inflammation. Therefore, Dietary Inflammatory Index (DII) has been proposed as an instrument that scores a potential of the diet, to cause inflammation based on its pro-inflammatory and anti-inflammatory foods and nutrients. Recently, molecular hydrogen therapy has been used for the treatment of NCDs due to its potential anti-inflammatory effects. It is possible that application of molecular hydrogen (H₂) in the foods can increase the anti-inflammatory potential of the diet leading to low DII, which may be protective against inflammation and related diseases.

Keywords: oxidative stress, peroxidation, inflammation, chronic diseases

Volume 15 Issue 1 - 2026

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Received: January 21, 2026 | **Published:** February 4, 2026

Introduction

Epidemiological studies indicate a comparative risk assessment of various risk factors or clusters of risks that may be associated with oxidative stress and inflammation.¹ Chronic low-grade inflammation is crucial in the pathophysiology of chronic non-communicable diseases (NCDs).²⁻⁴ Dietary Inflammatory Index (DII) has been proposed as an instrument that scores a diet's potential to cause inflammation based on its pro-inflammatory and anti-inflammatory foods and nutrients.^{5,6} A higher, more positive inflammatory index score indicates a more pro-inflammatory diet, such as a western-type diet, while a lower, more negative score suggests a more anti-inflammatory diet, such as Mediterranean type diet.^{7,8} More recently, application of molecular hydrogen (H₂) has been suggested to provide anti-inflammatory potential of the diet.^{9,10} Fruits, vegetables, nuts, and seeds are quite expensive, therefore, it is hypothesized that applying H₂ to foods may be an alternative strategy to enhance the anti-inflammatory index of the diet. This editorial aims to explore the role of H₂ as a potential anti-inflammatory agent for increasing the anti-inflammatory index of the foods, with reference to health and prevention of diseases.

Inflammation and risk of diseases

Chronic low grade inflammation is a slow, process lasting several months to years,³ which may a part of defense mechanism of the body, in which the immune system recognizes and removes harmful or foreign stimuli, initiating the healing process. Chronic inflammation, via multiple pathways, influences blood pressure, coagulation, and lipid profiles, serving as a significant risk factor for the onset of cardiovascular disease (CVD).²⁻⁴ Pro-inflammatory dietary patterns can exacerbate risk factors for CVDs and other chronic diseases by amplifying inflammatory mediators and metabolic factors, thereby increasing CVD outcomes.^{7,8} Current findings regarding the relationship between dietary habits and CVD risk factors, such as blood pressure, platelet function and lipid levels, exhibit considerable variability, which may be due to variations in the dietary inflammatory index.^{5,6} which may be accelerated due to circadian dysfunction.^{11,12}

Effects of western diet on inflammatory index

Western diets, characterized by High content of refined and processed foods, red meat, processed rich in salt, trans fat and sugar, are strongly linked to a higher dietary inflammatory index (DII) and chronic inflammation.^{5,6} Higher dietary inflammation has been found to be associated with a higher burden of multi-morbidity of cardio-metabolic and mental health disorders in an urbanizing community of southern India.^{7,8} These diets are associated with lower intake of anti-inflammatory foods such as vegetables, fruits, nuts, seeds, and whole grains. Therefore, a higher DII score is associated with an increased risk of chronic diseases, such as hypertension, metabolic syndrome, and certain cancers.^{8,14} Western diet, may cause inflammation, leading to oxidative dysfunction in the ultra-structure of tissues.^{7,8,11,14,15} The Mediterranean diet has a low inflammatory index and is associated with a lower risk of NCDs, while a western-type diet has a high inflammatory index and is linked to an increased risk of these diseases.^{8,16,17} This quality of the diet is provided by the Mediterranean type of foods which are rich in anti-inflammatory foods like fruits, vegetables, whole grains, and olive oil, while the western type of diet is characterized by pro-inflammatory foods.

Effects of Mediterranean type of foods on inflammatory index

The Mediterranean-style diet contain plant foods and olive oil with moderate dairy products and poultry and lower amount of animal foods such as red meat. Mediterranean-style diets focus on fruits, vegetables, whole grains, legumes, nuts, and seeds, using olive oil as the primary source of fat. It includes minimal amounts of animal products like poultry, fish, eggs, and dairy, little red meat, substituting spices and herbs for flavor rather than salt, and choosing whole, minimally processed foods. The Indo-Mediterranean diet is a plant-based diet that emphasizes whole grains, legumes, vegetables, nuts, seeds, and seasonal fruits, while minimizing or excluding processed foods and animal products, except for fish and other seafood, and dairy products in moderate amounts.^{9,14} It combines both the traditional Mediterranean diet and Indian cuisine, incorporating millets,

porridge, peas, and grams, along with spices such as turmeric, cumin, coriander, mint, fenugreek, cinnamon, cardamom, and cloves, which are typically prepared with healthy oils such as mustard, soybean, or olive oil. These diets are mainly plant-based, which are associated with lower morbidity and mortality.¹⁴

Possible effects of hydrogen-enriched foods on health

The oxidative function of the myocardial and other cells of the body, how oxidative dysfunction causes physio-pathological remodeling, leading to NCDs is not well known. Dietary antioxidants, such as polyphenolics and flavonoids, omega-3 fatty acids, and other micronutrients, including essential and nonessential amino acids, that are rich in high exogenous Indo-Mediterranean-type diets, may help sustain the oxidative functions of the heart, brain and other body systems.^{2-4,15} If the levels of these antioxidant nutrients are lower in tissues, oxidative stress and inflammation increase. The body's systems and tissues continue to use glucose and fatty acids for physiological functions, depending on tissue metabolic requirements; however, a deficiency in antioxidant nutrients predisposes cells to oxidative stress, leading to damage in various organs. It is possible that both gluco- and lipo-toxicity can damage cells, worsening in the presence of a deficiency of endogenous antioxidants, leading to an increased demand for exogenous antioxidant nutrients from the diet. In such situations, increased supply of hydrogen-enriched foods could be protective against oxidative stress and inflammation in the body tissues, because H₂ is a potential antioxidant and anti-inflammatory agent.^{9,10}

Hydrogen-enriched foods are products that were fortified with hydrogen gas inside them or packaged under a hydrogen-incorporated atmosphere.⁹ Consumption of hydrogen-treated foods provides nutritional adequacy and health. The enrichment methods include hydrogen gas infusion and the use of hydrogen-producing magnesium. The infusion method is especially applied for liquid foods, such as beverages while the hydrogen-producing magnesium is used for both liquid and solid foods. The enrichment of foods with hydrogen can also be achieved by packaging foods under a hydrogen-incorporated atmosphere, where hydrogen can be dissolved and diffused in the food matrix, including the aqueous and fat phases.⁹ This method is referred to in the literature as reducing atmosphere packaging (RAP). Another innovative technique used in food processing to enrich food with hydrogen is reducing atmosphere drying (RAD), in which the food product is dried under a hydrogen-containing atmosphere. Another emerging technique is the use of hydrogen-producing magnesium in the formulation of foods, such as minced meat or in the edible coatings and films of foods, such as meatballs.⁸ All the above innovative methods provide green, sustainable alternatives for enriching food with non-conventional antioxidants, with multiple advantages over traditional antioxidants, such as hydrogen gas.

Effects of hydrogen rich foods on autophagy and apoptosis

In addition, high-sugar and high-fat diets can increase the production of ceramide, advanced glycation end products (AGEs), and trimethylamine N-oxide (TMAO), which can predispose to oxidative dysfunction and Ca-overloading in cells, leading to apoptosis.^{11,15} Alterations in biology may begin with physiological cellular remodeling and progress to biological remodeling due to inflammation. It is proposed that a greater intake of hydrogen-enriched foods, which provide additional molecular hydrogen, may improve food quality,⁹ making them anti-inflammatory and increasing the diet's antioxidant potential. The beneficial effects occur by inhibiting

oxidative damage to lipids, proteins, and DNA in cells during the early stage of apoptosis, possibly due to hydrogen-induced autophagy.¹⁶ There is an unmet need to conduct cohort and randomized controlled studies using hydrogen-enriched foods to demonstrate the role of the anti-inflammatory index in the management of CVDs and other chronic NCDs.

Molecular hydrogen acts as a dual modulator of autophagy, either promoting or inhibiting it depending on the cell type, disease, stress severity, and duration.¹⁶⁻¹⁸ The primary mechanism involves counteracting oxidative stress, inflammation, and apoptosis, which in turn influences the cellular need for autophagic regulation to maintain homeostasis.¹⁶ Alwazeer and co-workers reported that hydrogen is a potential green alternative to chemical fertilizers, which are known to increase yield without improving food quality.⁹

Beneficial uses of molecular hydrogen and its pharmacokinetics

In health and diseases, hydrogen supplementation is made via inhalation, HRW, hydrogen-rich saline, hydrogen-rich eye drops, and hydrogen-rich bathing. Hydrogen as nutritional therapy can be applied to a variety of diseases, because it offers a natural alternative to chemical and radiation therapies.¹⁹ A previous study on the pharmacokinetics of hydrogen in pigs showed that ingesting an HRW results in rapid, high concentrations in the jejunal vein, reaching peak levels within minutes.¹⁹ Hydrogen then distributes through the portal vein, inferior vena cava, and to a much lesser extent, in the carotid artery. Concentrations in the jejunal and portal veins decrease over time but may remain elevated beyond 2 hours, whereas concentrations in the carotid artery remain low. The highest hydrogen concentrations were observed in the jejunal vein, with levels peaking at approximately 0.276 mg/L.¹⁹

Hydrogen water enhances oxygen saturation in patients with chronic lung disease.¹⁷ It is proposed that, despite low hydrogen concentration, it may trigger vascular NO generation. In the gut, it may regulate gut microbiota function, leading to increased production of short chain fatty acids (SCFA), brain derived neurotrophic factor (BDNF) and anandamides with greater sparing of nitrite. In other organs, such as brain, heart, liver, vessels, kidney, muscle, pancreas, hydrogen therapy may enhance autophagy, leading to improved function of cardiac cells, neurons, hepatocytes, vascular endothelial cells, beta cells of the pancreas, osteocytes, and adrenals.¹⁶⁻¹⁸ Application of H₂ in the alcohol or wine can further cause increase in the anti-inflammatory index of the wine which is known to cause significant decline in mortality.²⁰

Conclusion

DII has been proposed as an instrument that can score a diet's potential to cause inflammation based on its pro-inflammatory and anti-inflammatory components. A higher, more positive inflammatory index score indicates a pro-inflammatory western-type diet, while a low score suggests a high anti-inflammatory, nutrient-rich diet. Since hydrogen is a potential anti-inflammatory agent, application of molecular hydrogen in the foods has been found to enhance anti-inflammatory potential of the diet. Fruits, vegetables and nuts and seeds are quite expensive, therefore hydrogen application in the foods as an alternative strategy may be considered to enhance the anti-inflammatory index of the diet.

Acknowledgments

None.

Conflict of interest

The authors declare that there is no conflict of interest.

Funding

None.

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