

Wound healing properties of the Mediterranean diet

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Abstract

The Mediterranean Diet has proven itself effective in acute and chronic wound healing. A Mediterranean diet includes whole grains, vegetables, fruits, fish, olive oil, red wine, and legumes. Foods studied within this diet contain high levels of antioxidants and anti-inflammatory compounds. The diversity of foods and numerous nutritional benefits maximizes wound healing with a variety of protective substances. The Mediterranean Diet has high concentrations of polyphenols, carotenoids, vitamins, and flavonoids. Additionally, foods found within the Mediterranean diet are high in protein, zinc, vitamin A, and vitamin C, which specifically aid in wound healing and the body's defenses against infection. A low sodium Mediterranean Diet has also been found to strengthen the activation of macrophages to increase the tissue inflammation process and promote wound healing. The consumption of olive oil has been found to lower the incidence of dermatological diseases. Specifically, olive oil also plays an important role in increased platelet function thus having a direct effect on wound healing and decreased inflammation. Our review addresses how a Mediterranean Diet aids with acute and chronic wound healing. The impact of nutrition on wound healing from a Mediterranean Diet allows for development of a nutritional approach to minimize incidence of acute or chronic, non-healing wounds via dietary changes.

Key words: physiological mechanisms; nutrition; cardiovascular and metabolic diseases

Introduction

The pivotal role of nutrition in influencing various aspects of health has long been acknowledged in scientific literature, and recent attention has turned towards exploring the impact of specific dietary patterns on wound healing [1,2]. Among these, the Mediterranean diet has garnered considerable interest due to its holistic composition, emphasizing the consumption of whole grains, vegetables, fruits, fish, olive oil, red wine, and legumes. Despite its well-established preventative effects on cardiovascular and metabolic diseases, little attention has been paid to its role in wound healing. However, with wounds affecting 15% of patients and costing more than 28 billion dollars annually, it highlights a significant burden on individuals, healthcare providers, and facilities alike [3]. Given this, there is a crucial need for further research exploring the integration of a Mediterranean diet into wound care management, offering a potential holistic approach to the complexities associated with wound care. This paper aims to examine the scientific evidence surrounding the effectiveness of the Mediterranean diet in acute and chronic wound healing, evaluating the biochemical and physiological mechanisms that underlie its observed therapeutic effects.

Central to the appeal of the Mediterranean diet are its unique combination of nutrients, including high levels of antioxidants, anti-inflammatory compounds, polyphenols, carotenoids, vitamins, and flavonoids. Beyond its established benefits for cardiovascular and metabolic health, the diverse nutritional composition of this diet shows significant promise for enhancing wound-healing outcomes [1,4].

As the Mediterranean diet gains recognition for its nutrient-rich profile, attention has turned to specific micro- and macronutrients contributing to its wound-healing properties. Proteins, abundant in lean meats, seafood, eggs, beans, nuts, and soy derivatives within the Mediterranean diet, play a fundamental role in tissue repair. This paper examines studies demonstrating the beneficial effects of protein intake on wound healing, emphasizing its role in accelerating the healing process. Additionally, the trace mineral zinc, prevalent in red meats, poultry, lentils, and fruits like pomegranates within the Mediterranean diet, emerges as a critical factor in maintaining epithelial and tissue integrity [5]. The research presented here showcases the implications of zinc deficiency on chronic wounds and explores the potential of dietary zinc to prevent deficiency-related complications and expedite wound healing.

Furthermore, the presence of essential vitamins within the Mediterranean diet reveals key contributors to wound healing [6]. Notably, vitamin A and vitamin C cannot be overlooked. Vitamin A, abundant in leafy green vegetables, tomatoes, and various fruits, plays a central role in epidermal turnover and re-epithelialization. This paper further examines studies investigating the effects of vitamin A on wound healing, shedding light on the mechanisms by which it activates critical genes for tissue repair. Moreover, vitamin C, another vital component found in abundance in the diet's fruits and vegetables, emerges as a crucial cofactor in collagen synthesis. Clinical trials evaluating the impact of vitamin C supplementation

on chronic foot ulcers are discussed, emphasizing the potential role of a well-balanced Mediterranean diet in providing adequate levels of this vitamin for optimal wound healing.

Additionally, this introduction underscores the diet's low sodium content as a facilitator of wound healing. By contrasting it with the prevalent high-sodium Western diet, our discussion will further explore how reduced sodium intake potentially augments macrophage activation and bolsters the body's innate immune response, thereby enhancing wound healing capabilities [7]. Further contributing to the Mediterranean diet's therapeutic profile is the inclusion of olive oil, a staple extending beyond culinary applications. Rich in omega-3 polyunsaturated fatty acids and polyphenols, olive oil's impact on platelet function and dermatological health will be evaluated, emphasizing its potential in modulating inflammation and fostering expedited wound recovery [8].

The Mediterranean diet emerges as a powerful therapeutic approach in wound care, utilizing its diverse nutritional elements to optimize physiological healing processes. Supported by evidence-based research and clinical insights, this dietary paradigm not only emphasizes the mechanisms of wound repair, but also underscores the potential for integration as an adjunctive treatment option in advanced wound management protocols.

Discussion

A Mediterranean diet is beneficial in wound healing due to the unique properties of the diet and the variety of nutrients they contain. The Mediterranean diet emphasizes the intake of fruits, vegetables, legumes, nuts, whole grains, fish and olive oil with limited meat consumption and alcohol intake in the form of wine [9]. The Mediterranean diet is well regarded in its cardio- and chemo-protective properties, in part due to the high antioxidant composition of the foods consumed. In this study, the wound healing properties of the Mediterranean diet will be discussed.

Protein

Protein can be found in lean meats, seafood, eggs, beans, nuts and soy derivatives and comprises a large component of the Mediterranean diet. An animal-model study by Tsuda et al. built an experiment around rats fed a protein-free and protein-fed diet to analyze wound healing in an all-layer skin defect and found that protein incorporation into the diet at any time during wound healing accelerated the process and was most effective with early intervention [10]. An evidence-based analysis by the medical secretariat in 2008 looked at the treatment of chronic pressure ulcers and found that those given a very high concentration feeding tube of protein (25% concentration protein) had greater reduction in ulcer area than those given a high concentration feeding tube of protein (16% concentration protein) [11]. While attributions to increased protein supplementation in diet had been linked to better wound healing, the exact mechanism has not been discovered. A study by Yamane et al. analyzed the quality of protein and fed a rat group a gluten heavy diet that resulted in upregulation of metalloproteinase (MMP) 2 protein which had negative effects on wound healing [12]. While more research needs to be done, this demonstrates that whole protein from lean and natural sources as found in the Mediterranean diet can lead to improved wound healing in the patient.

Zinc

Zinc is a trace mineral with highest concentrations found in oysters, but also plentiful in red meats, poultries, lentils and fruits such as pomegranates—all mainstays of the Mediterranean diet. Zinc helps to maintain epithelial and tissue integrity through its free radical mechanism to inhibit apoptosis and promote angiogenesis [13]. A case report by Perafan-Riveros et al. described a case of acrodermatitis enteropathica, an intestinal absorption disorder leading to impaired absorption of zinc that can present with chronic wounds. This case showed significant improvement of skin lesions with 40 mg/day zinc supplementation in the zinc-deficient patient, indicating the crucial role zinc can play in prompt wound healing [14]. Zinc has a large component stored in the skin, so the presence of a wound directly eliminates those zinc

stores in addition to overall zinc stores being depleted leading to overall deficiency [15]. Incorporation of zinc through foods consumed in the diet, particularly those included in the Mediterranean diet, could prevent patients from reaching deficiency and being susceptible to wound formation as well as aid in healing process however more studies need to be performed.

Vitamin A

Vitamin A is mainstay of skincare due to its powerful effects of epidermal turnover and re-epithelialization, which inherently makes it beneficial to wound healing. Vitamin A can be found in leafy green vegetables, tomatoes, yellow vegetables and fruit including sweet potatoes, cantaloupe, and mango. An experimental study by Lee et al. studied the use of topical Retinoic acid in wound healing and found that wound healing significantly improved due to the mechanism of activating *Arg1*, which is a critical gene for tissue repair in macrophages [16]. There are far fewer studies exploring intrinsic levels of vitamin A or how vitamin A supplementation can affect wound healing. A study by Levenson et al. looked at how vitamin A supplementation in rats post-acute radiation injury, including impaired wound healing and gastrointestinal ulceration, and found that wound healing was not impaired in rats supplemented with Vitamin A, and supplementation was no more or less effective whether supplemented before or after radiation [17]. Researchers postulated that supplementation of vitamin A aiding in wound healing by increased the inflammatory cells at the cite, modulating collagenase activity and inducing epithelial cell differentiation. More studies need to be conducted on parameters for supplementation and dosing because the adverse effects of too much vitamin A can led to toxicity and potentially death in patients. Looking for vitamin A in sources from your diet, as found by choosing nutrient rich foods in the Mediterranean diet could eliminate the need for supplementation and maintain stores optimal for wound healing.

Vitamin C

Vitamin C, also known as ascorbic acid, is a water-soluble vitamin found in abundance in fruits, specifically citrus foods and vegetables, and plays an important role in skin integrity. Vitamin C is a cofactor in the synthesis of collagen, a structural protein found in abundance in the skin [18]. A study by Gunton et al., evaluated 500 milligrams (mg) of slow-release oral vitamin C in a double-blind randomized control trial on chronic foot ulcers and found that healing at eight weeks was significantly improved in the vitamin C group [19]. It was also found during the study that half of participants had a vitamin C deficiency at baseline, which was corrected for [19]. The authors of this study concluded with a recommendation that vitamin C therapy should be offered to patients with chronic foot ulcers and suboptimal vitamin C intake [19]. With a well-balanced diet such as with the Mediterranean diet, adequate levels of vitamin C will be consumed, which can further facilitate wound healing.

Phytochemicals

Phytochemicals are found in abundance in the Mediterranean diet, as fruits and vegetables are one of the main cornerstones of the diet. Specifically, the cucumber fruit contains ethyl acetate and methanol extracts which contain antimicrobial properties, while anthocyanin found in various berries (such as strawberries, red raspberries, and sweet cherries) and red onions also exhibits these properties [18]. Resveratrol, found in abundance in wine which is consumed in moderation as part of the Mediterranean diet, aids in the promotion of wound healing [18]. Phytochemicals, found commonly in vegetables, may play an important role in wound healing to aid in infection prevention during this process.

Low Sodium

A major factor in the Mediterranean diet is low sodium, especially when compared to the modern Western diet that boasts large amounts of sodium, specifically in pre-packaged foods. The current recommendation from the American Heart Association (AHA) is to limit sodium consumption to no more than 2,300 mg in a day, currently moving towards an ideal intake of no more than 1,500 mg a day. Wound healing is diminished in a high-sodium diet due to the inhibition of macrophage differentiation; in this environment

there is an increase of the development of pro-inflammatory M1 macrophages and Th17 cells and an inhibition of regulatory M2 macrophages and T regulatory cells [20]. Adhering to the Mediterranean diet aids in wound healing via the innate and adaptive immune response by decreasing the amount of sodium consumed.

Olive Oil

The main source of fat in the Mediterranean diet is olive oil, which is rich in omega-3 polyunsaturated fatty acids and polyphenols. A byproduct of olive oil production is alperujo extract, which contains hydroxytyrosol and 3,4-dihydroxyphenylglycol (DHPG), which modulates platelet function [21]. A study by De Roos, et al., evaluated the byproduct of olive oil containing these compounds and found that alperujo extract significantly inhibited collagen-induced platelet aggregation and thrombin receptor analogue peptide-induced platelet aggregation at certain concentrations *ex vivo* [21]. In wound healing, platelets have a vital function in wound hemostasis and healing; this compound may protect against platelet aggregation. More research should be conducted in this area, specifically *in vivo* studies. Olive oil byproducts are often wasted; if there are beneficial effects of the byproduct, they could be incorporated into the diet.

Conclusion

In conclusion, the Mediterranean diet and its impact on wound healing underscores the scientific merit and potential clinical implications of this dietary pattern. The Mediterranean diet, characterized by the consumption of whole grains, vegetables, fruits, fish, olive oil, red wine, and legumes, emerges as a potent aid in both acute and chronic wound healing. The diverse array of nutrients within this diet, such as antioxidants, anti-inflammatory compounds, polyphenols, carotenoids, vitamins, and flavonoids, collectively contribute to a synergistic effect that maximizes the body's natural healing processes. The inclusion of essential elements like protein, zinc, vitamin A, and vitamin C further supports the diet's role in promoting wound healing and bolstering the body's defenses against infection. The low sodium content in the Mediterranean diet enhances the activation of macrophages, crucial for the tissue inflammation process and overall wound healing. Olive oil, a prominent component of this diet, not only lowers the incidence of dermatological diseases but also influences platelet function, thereby directly impacting wound healing and mitigating inflammation. In light of these findings, a nutritional approach centered around the Mediterranean diet emerges as a promising strategy to minimize the incidence of acute or chronic non-healing wounds, offering a scientifically grounded and holistic perspective on the crucial interplay between nutrition and wound healing. Further research and clinical trials are warranted to better understand specific mechanisms, optimal dosages, and potential therapeutic applications for this dietary approach in wound care.

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