

The Potential of Nutraceuticals for Age Related Macular Degeneration (AMD)

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Abstract

Age related macular degeneration (AMD) is a serious threat to public health as it is the leading cause of visual loss, and its prevalence is predicted to rise considerably. While current treatment options exist for advanced stages, there is a compelling need to explore preventative and management strategies. This review investigates the potential of nutraceuticals in mitigating AMD progression. We explore the proposed mechanisms of action by which specific nutraceuticals may counteract oxidative stress, inflammation, and other detrimental factors. The Age Related Eye Disease Study (AREDS) and AREDS2 are two important clinical research studies that are looked at to show how certain formulations with antioxidants and minerals can help people. Furthermore, we delve into emerging evidence on the potential of promising. This review underscores the potential of nutraceuticals as a complementary approach for managing AMD, emphasising the need for further research to optimise their efficacy and personalise treatment plans for individual patients.

Keywords: Age-related macular degeneration (AMD); Nutraceuticals; Lutein; Zeaxanthin; Oxidative stress; Inflammation.

INTRODUCTION

AMD is a devastating eye disease that affects the macula, a critical area of the retina crucial for precise central vision.¹⁻⁵ It is a significant cause of blindness, especially among the elderly, and affects millions of people worldwide.¹ The gradual pattern

of vision loss makes observing and managing AMD difficult.⁶⁻¹¹

A. Types of AMD

There are two primary subtypes of AMD categorised based on their underlying pathology, severity, and clinical presentation: “wet” (neovascular or exudative) and “dry” (atrophic) AMD.^{2,8,12} While they share some characteristics, dry AMD progresses more gradually and can ultimately lead to blindness.² The location, size, and number of drusen are crucial indicators of AMD severity and potential vision loss.³

B. Challenges and Need for Nutritional Intervention

Unfortunately, previous research hasn't established optimal dosages or specific nutrient combinations for treating AMD and other eye

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conditions.⁴ Many patients, seeking relief, resort to over-the-counter supplements without proper guidance.⁴ This highlights the critical need for scientific and medical expertise to inform patients and consumers about potentially beneficial dietary strategies.¹³⁻¹⁸

C. Focus of this Review

This review focuses on the well-studied dietary approach for treating and preventing AMD and other eye-related disorders. In this article, researchers discuss the potential benefits of a number of different nutrients, such as zinc, selenium, anthocyanins, and vitamins A, C, and E.¹²⁻²⁰ Among these, zeaxanthin and lutein stand out as potent antioxidants with the potential to lower the risk of AMD and other eye diseases.⁵ Vitamins C and E also play a role, while vitamin A holds particular importance for the human retinal pigment epithelium.^{5,8}

Types of Macular Degeneration

AMD, also referred to as macular degeneration, affects the macula, which is the central region of the retina and crucial for precise central vision.¹ Apparently, dry AMD and wet AMD are the two main classifications that are used for describing AMD.^{1,20}

A. Dry AMD (Non-neovascular AMD)

Approximately 80–90% of all instances of macular degeneration have dry AMD. Thus, this renders dry AMD the most prevalent form of macular degeneration.² It is considered a gradual deterioration of macular tissue as the cells in the macula degenerate over time.² Deposits known as drusen, composed of yellowish extracellular material, often accumulate behind the retina in dry AMD.^{2,8} Dry AMD typically progresses slowly and can lead to a progressive decline in central vision.²⁰ Recent clinical trials that focused on complement system modulators have shown negative results, which suggests that therapy may not be able to help at this point.³ These failures may be attributed to similar reasons as observed in other degenerative diseases of the degenerative diseases of the central nervous system. Treatment may be initiated too late in the disease cascade, after a point of no return has been reached. There are currently no known tactics to prevent additional photoreceptor loss along the borders of the atrophic areas in the macula. In such circumstances, irreversible damage has already occurred to neural tissue, particularly retinal photoreceptors. This causes the retina to progressively lose its ability to perceive light.³

B. Wet AMD (Neovascular AMD)

Wet AMD, constituting 10–15% of all AMD cases, is less common but presents a more severe form of the disease.² These aberrant blood vessels are fragile and prone to bleeding, further exacerbating vision loss through scar tissue formation.² Wet AMD can manifest with sudden changes in vision, including distortion or a black spot in the centre of the visual field.² Wet age-related macular degeneration can rapidly proceed and result in permanent visual loss if it is not addressed.² Over the past several years, there has probably been a major rise in the number of people who are blind or have serious vision impairments. Data from Germany and other countries reveal that despite a discernible increase in the frequency of AMD, rates of blindness and severe visual impairment have remained consistent or even decreased.^{4,8} This is the case, despite the fact that the prevalence of AMD has increased. This pattern is most certainly attributable, at least in a significant degree, to the effective launch of a treatment in 2005 for the most severe form of age-related macular degeneration, which is known as exudative late type.^{4,20} This recognition was based on the findings of two successful phase 3 clinical studies. Intravitreal injections are where anti-VEGF medications are given to patients. These injections are given directly into the vitreous body of the eye. Ranibizumab, which was authorised in 2007, aflibercept, which was approved in 2012, brolicizumab, which will be approved in 2020, and bevacizumab, which has been used off-label since 2005, are the four medications that are now accessible for commercial usage with these characteristics.^{4,8}

C. Causes and Risk Factors

Age-Related Macular Degeneration (AMD): Risk Factors

- **Chronological Ageing:** The most prominent risk factor for AMD is advancing age.¹ The macula, a region of the retina with high metabolic activity, places a significant cumulative burden on the retinal pigment epithelium (RPE) for waste product clearance throughout life.¹ With senescence (cellular ageing), the RPE's capacity for phagocytosis (waste removal) diminishes, potentially contributing to AMD pathogenesis.¹
- **Smoking:** A modifiable risk factor, cigarette smoking significantly increases the risk of developing AMD.¹ Compared to non-smokers, smokers exhibit elevated risk ratios ranging from 2.6 to 4.8.¹ Notably, even smoking cessation does not entirely eliminate

the risk, with former smokers having a 1.7-fold higher risk than those who never smoked.¹

- **Genetic Predisposition:** Recent research has identified several genetic polymorphisms associated with AMD susceptibility, including those linked to smoking behavior.¹ Changes in the complement factor H (CFH) and age-related maculopathy susceptibility 2 (ARMS2) genes are especially important because they may explain up to 45% of the overall risk of AMD.¹
- **Potential Associations with Other Conditions:** Studies suggest possible correlations between AMD and various health conditions, including:
 - Body mass index (BMI)^{1,10}
 - Cardiovascular disease (CVD)^{1,20}
 - Arterial hypertension (high blood pressure)^{1,20}
- **AMD and Atherosclerosis: A Tentative Link** Research investigating the potential connection between AMD and atherosclerosis (arterial wall thickening) yields inconclusive results, but some intriguing similarities exist.^{2,4} Drusen, hallmark deposits found in AMD, share certain characteristics with atherosclerotic plaques observed in the arteries of individuals with high cardiovascular risk.^{2,4}

Nutraceuticals and Amd

Nutraceuticals, a blend of “nutrition” and “pharmaceutical,” encompass food or food components with potential health benefits. They offer a natural and potentially complementary approach to managing AMD.^{8,20}

A. Mechanisms of Action:

Several methods have been proposed to explain how nutraceuticals may assist AMD sufferers.

- **Antioxidant Effects:** AMD is linked to oxidative stress, which damages retinal cells. Nutraceuticals having antioxidant characteristics, such as vitamins C and E and carotenoids (lutein and zeaxanthin), may help neutralise free radicals and preserve retinal tissue.^{8,19}
- **Anti-inflammatory effects:** Chronic inflammation is linked to AMD development. Anti-inflammatory nutraceuticals such as omega-3 fatty acids and curcumin may aid in reducing inflammation and protecting retinal

cells.^{8,19}

- **Modulating Cell Signalling Pathways:** Certain nutraceuticals, such as zinc and vitamins, may impact cellular signalling pathways that contribute to AMD progression.^{8,19}

B. Clinical Evidence

- **The Age-Related Eye Disease Study (AREDS) and AREDS 2:** Landmark studies showed that certain nutraceutical formulations with high doses of antioxidant vitamins (C and E) and zinc greatly lower the risk of progressing to advanced AMD in people who already have intermediate or advanced AMD in one eye.^{8,13,19}
- **Lutein and Zeaxanthin:** Recent studies suggest a potential preventive role for carotenoids in age related macular degeneration (AMD) due to their high macular concentration and capacity for blue light filtration.^{8,13,19}
- **Other Nutraceuticals:** Another investigation is being carried out on nutraceuticals like omega-3 fatty acids and coenzyme Q10 to determine their specific function in managing AMD. However, additional studies are required to demonstrate their conclusive impact.

Key Dietary Factors Associated with Nutraceuticals in the Context of Macular Degeneration Include

Antioxidants: Dietary antioxidants play a crucial role in protecting the retinal pigment epithelium (RPE) from oxidative stress, a well-established contributor to the pathogenesis of age related macular degeneration (AMD).¹ Nutraceuticals enriched with antioxidants, particularly vitamins C and E, zinc, and selenium, possess the potential to neutralise free radicals and minimise oxidative damage within the macula.^{5,8,13,19}

Omega-3 Fatty Acids: The omega-3 fatty acids docosahexaenoic acid (DHA) and eicosatetraenoic acid (EPA) are particularly abundant in fatty fish like salmon and trout, which are considered to be among the best sources of oil. It has been suggested that these fatty acids may have positive effects on eye health, including the reduction of inflammation and the maintenance of the structure of the retina.^{8,13,19,20}

Lutein and Zeaxanthin: A. Lutein and zeaxanthin are carotenoids that are found in leafy green foods such as spinach and kale. These carotenoids concentrate in the retina, particularly in the macula.

By functioning as antioxidants and assisting in the filtering of potentially hazardous high-energy light waves, these chemicals have been speculated to have a role in the prevention of macular degeneration.^{8,13,19}

Vitamins: Micronutrients such as vitamins A, C, and E play essential roles in maintaining overall ocular health. Vitamin A, in particular, is critical for optimal retinal function.^{8,13,19}

Zinc: Maintaining adequate zinc homeostasis is crucial for retinal health. Studies have investigated zinc supplementation as a potential intervention to slow the progression of age-related macular degeneration (AMD).^{8,13,19}

Age-Related Macular Degeneration: The Role of Supplementation and Diet

AMD, particularly the dry form, remains a significant challenge for ophthalmologists and researchers.¹ Despite numerous clinical trials, there is currently no known cure for this progressive retinal disease.¹ However, modifiable factors like diet and supplementation can significantly impact AMD incidence and progression.^{2,8,13,19}

Table 5. 1. Nutrient Composition of Commercially Available Formulas Based on the Age-Related Eye Disease Study (AREDS/AREDS2)

Nutrient	AREDS Formula (Age-Related Eye Disease Study)	AREDS2 Formula (Age-Related Eye Disease Study 2)
Vitamin C	500 mg	500 mg
Vitamin E	400 IU	400 IU
β-Carotene	15 mg	Not Included
Lutein	Not Included	10 mg
Zeaxanthin	Not Included	2 mg
Zinc	80 mg	80 mg
Copper	2 mg	2 mg

Sources: National Eye Institute. (n.d.). Facts about age-related macular degeneration. National Institutes of Health (gov): <https://www.ncbi.nlm.nih.gov/books/NBK560778/>.⁸

Dietary Considerations for Amd

Diet is undeniably a vital factor in AMD management.² Appropriate nutritional counselling is recommended for individuals at risk.² Here are some key dietary principles:

Improve Diet Quality: Dietary Recommendations for Age-Related Macular Degeneration (AMD): Age related macular degeneration (AMD) is a leading cause of vision loss in older adults. While there is no cure, a well-balanced diet rich in certain fruits,

vegetables, and whole grains can play a significant role in managing AMD and potentially slowing its progression. Here's a breakdown of key dietary recommendations:

Prioritise Fruits and Vegetables: Consume a rainbow of fruits and vegetables throughout the day to benefit from a wide range of antioxidants and other protective nutrients.

Leafy greens are champions. Focus on dark leafy greens like spinach, kale, and collard greens, which are rich in lutein and zeaxanthin, carotenoids crucial for macular health.¹

Other beneficial choices: Include orange and yellow vegetables like carrots, peppers, and sweet potatoes, as well as berries and citrus fruits, all rich in vitamins and antioxidants.

Embrace Whole Grains: Choose whole grains over refined grains. Whole grains provide fibre, which can help with overall health and potentially reduce inflammation, a factor in AMD development.²

Examples: brown rice, quinoa, whole wheat bread and pasta, and oats.

Limit pro-oxidative foods:

Minimise saturated and trans fats. These fats can contribute to inflammation, potentially worsening AMD.

Reduce processed foods: Limit processed foods, sugary drinks, and excessive red meat, as these may contribute to oxidative stress.

Additional Considerations

Prioritize Retinal Nutrients: Increase consumption of foods rich in lutein, zeaxanthin, omega-3 fatty acids, vitamins C and E, and zinc.² Examples include leafy green vegetables, eggs, fatty fish, and nuts.^{9,13,19}

Limit Pro-Oxidative Foods: Reduce intake of processed foods, saturated and trans fats, and refined carbohydrates, which can contribute to oxidative stress.²⁰

Growing need for dialysis intervention

It is anticipated that the number of AMD sufferers will dramatically increase as the population of the world continues to age.¹⁰ Healthcare professionals can play a proactive role by promoting dietary choices that minimise AMD risk and empower patients to manage this sight threatening condition.¹⁰

Considerations and Future Directions

Individualised Approach: The optimal nutraceutical combination may vary depending on an individual's specific needs and risk factors.

Safety and Dosage: A. High dosages of nutraceuticals may cause negative effects. Medical professionals should be consulted for dosage and drug interactions.

Future Research: More research is needed to explore the efficacy of various nutraceuticals, identify optimal formulations, and understand long-term safety profiles.

CONCLUSION

Certain dietary supplements have been shown to help manage AMD in clinical trials. The current AMD supplement includes antioxidants, zinc, and macular pigment carotenoids. However, further investigation is needed to optimise the dosage and combination of nutrients within the AREDS2 formula, ensure long-term safety and efficacy data, explore emerging micronutrients like omega-3 fatty acids and resveratrol, and develop personalised medicine approaches. New research directions include exploring the role of gut microbiota in AMD development and understanding gene-nutrient interactions that influence AMD risk and response to supplementation. Further research is needed to fully understand these potential benefits.

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