

A review of the evidence germane to the putative protective role of the macular carotenoids for age-related macular degeneration

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Introduction

There is a consensus that age-related macular degeneration (AMD) is the result of (photo)-oxidative-induced retinal injury and its inflammatory sequelae, the latter being influenced by genetic background. The dietary carotenoids, lutein (L), zeaxanthin (Z), and meso-zeaxanthin (*meso*-Z), accumulate at the macula, where they are collectively known as macular pigment (MP). The anatomic (central retinal), biochemical (antioxidant) and optical (short wavelength-filtering) properties of this pigment have generated interest in the biologically plausible rationale that MP may confer protection against AMD.

Methods. A literature review was conducted to explore the evidence germane to the putative protective role of the macular carotenoids for AMD. The types of evidence considered eligible for inclusion in the review are summarised in Table 1

Results. The study details and principal findings in relation to macular carotenoids and AMD, of all studies included in the review, are summarised in Table 2

Table 1. Levels of evidence for therapy or prevention

Level	Type of study
1a	Systematic review (homogeneous) of RCTs
1b	Individual RCT (with narrow confidence interval)
2a	Systematic review of (homogeneous) cohort studies
2b	Individual cohort study / Low quality RCT
3a	Systematic review of (homogeneous) case-control studies
3b	Individual case-control studies
4	Case series, low-quality cohort or case-control studies
5	Expert opinions without explicit critical appraisal, or based on physiology, bench research or "first principles"

Material adapted from the recommendations for evidence-based medicine in Oxford.
<http://www.cebm.net/index.aspx?o=1025>

Table 2. Studies investigating the relationship between the macular carotenoids and age-related macular degeneration

Interventional Studies							
Principal Author	Study	Year	n	Study Design	Age	Carotenoids	Finding
Richer et al	-	1999	14	Case Series	61-79	L (14mg)	Improved VP
Olmedilla et al	-	2001	5	Case Series	69-75	L (15mg)	Improved VP
Richer et al	LAST	2004	90	RCT	68-82	L (10mg)	Beneficial‡
Bartlett et al	-	2007	25	RCT	55-82	L (6mg)	No benefit
Chakravarthy et al	CARMA	2007	433	RCT	50+	L (12mg) & Z (0.6mg)	Beneficial‡
Observational Dietary Studies							
Principal Author	Study	Year	n	Study Design	Age	Carotenoids	Nutrient/AMD relationship
Seddon et al	EDCCS	1994	356/520*	Case Control	55-80	L&Z	Inverse
VandenLangenberg et al	BDES	1996	1968	Cohort	45-86	L&Z	None
Mares-Perlman et al	NHANES III	2001	8222	Cross-sectional	40+	L&Z	Inverse
Flood et al	BMES	2002	2335	Cohort	49+	L&Z	None
Snellen et al	-	2002	72/66*	Case Control	60+	L	Inverse
LaRowe et al	CAREDS	2006	1787	Cross-sectional	50-79	L&Z	None
San Giovanni et al	AREDS	2007	4519	Case Control	60-80	L&Z	Inverse
Tan et al	BMES	2007	2454	Cohort	49+	L&Z	Inverse
Observational Serum Studies							
Principal Author	Study	Year	n	Study Design	Age	Carotenoids	Nutrient/AMD relationship
-	EDCCS	1993	421/615*	Case Control	-	L&Z	Inverse
Mares-Perlman et al	BDES	1995	167/167*	Case Control	43-86	L&Z	None
Mares-Perlman et al	NHANES III	2001	8222	Cross-sectional	40+	L&Z	Inverse
Simonelli et al	-	2002	48/46*	Case Control	mean=67	L&Z	None
Gale et al	-	2003	380	Cross-sectional	66-75	L&Z; L; Z	Inverse (Z only)
Cardinault et al	-	2005	34/21*	Case Control	72-74	L; Z	None
Delcourt et al	POLA	2006	899	Cohort	60+	L&Z	Inverse (esp. Z)
Fletcher et al	EES	2008	2283/2117*	Cross-sectional	65+	L; Z	Inverse (esp. Z)

Carotenoids = Macular carotenoids assessed in the study; L = Lutein; Z = Zeaxanthin; VP = Visual Performance; n = Number of subjects participating in study; Age = Age range (years) of subjects in study; RCT = Randomised control trial; EDCCS = Eye Disease Case Control Study; BDES = Beaver Dam Eye Study; NHANES = National Health and Nutrition Examination Survey; BMES = Blue Mountains Eye Study; CAREDS = Carotenoids in Age-Related Eye Disease Study; AREDS = Age-Related Eye Disease Study; POLA = Pathologies Oculaires Liées à l'Age; EES = European Eye Study; - = data unavailable.

*cases/controls

‡beneficial effect of supplementation



Conclusion

Level 1 evidence has shown that dietary supplementation with broad-spectrum antioxidants results in risk reduction for AMD progression. Studies have demonstrated that MP rises in response to supplementation with the macular carotenoids, although level 1 evidence that such supplementation results in risk reduction of AMD and/or its progression is still lacking. Although appropriately weighted attention should be accorded to higher levels of evidence, the totality of available data should be appraised in an attempt to inform professional practice. In this context, the literature demonstrates that supplementation with the macular carotenoids is probably the best means of fortifying the antioxidant defenses of the macula, thus putatively reducing the risk of AMD and/or its progression.

